IULIA CREȚU ILEANA CORNELIA FĂRCĂȘANU

COMPOUNDS WITH MIXED FUNCTIONAL GROUPS

PROBLEMS AND EXERCISES

Editura Universităţii din Bucureşti

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STEREOCHEMISTRY

1. Define the terms:
   a. enantiomer
   b. stereogenic center
   c. racemic modification
   d. diastereoisomer
   e. constitution
   f. conformation

   Give an example for each.

2. Classify the stereoisomers. Do they differ in constitution?

3. Mention one important experimental and one important conceptual discovery of Louis Pasteur's.

4. What did Jean Baptist Biot discover?

5. A sample of 0.3g diluted to 15mL is placed in a tube that is 1dm long. The observed rotation is $+1.72^{\circ}$. What is the specific rotation at 20°, Na D-line?

6. A pure enantiomer has the specific rotation $158^{\circ}g^{-1}mL\ dm^{-1}$. What will be the specific rotation of the mixture containing:
   a. 25% (+) enantiomer and 75% (-) enantiomer
   b. 50% (+) enantiomer and 50% (-) enantiomer
   c. 75% (+) enantiomer and 25% (-) enantiomer

7. The solvolysis of 2-bromooctane follow a SN_1- like mechanism, but when a single enantiomer is used as substrate, the product mixture is found to have a significant amount of optical activity, indicating that the mechanism does not involve full racemization.the specific rotation of (S)+ - 2-octanol is 89 and the mixture after solvolysis has an apparent specific rotation of +59. What percentage of the reaction is proceeding through a mechanism involving stereochemical inversion? Write the reaction.

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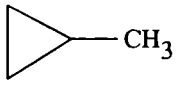
8. Give an example of a chiral compound which is not asymetric.

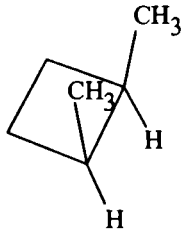
9. For compounds of the same constitution are there some which:

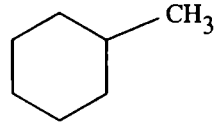
   a. Display enantiomerism but no diastereoisomerim?
   b. Display diastereoisomerism but no enantiomerism?
   c. Display both diastereoisomerism and enantiomerism?

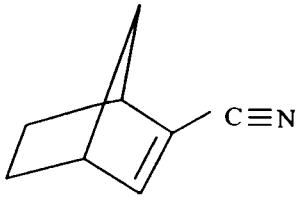
   Give examples for each.

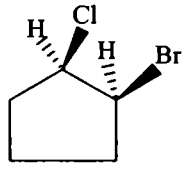
10. Determine which C atoms are chiral in the following compounds:

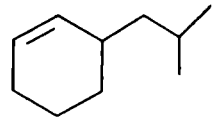
a. 

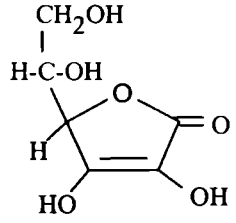
b. 

c. 

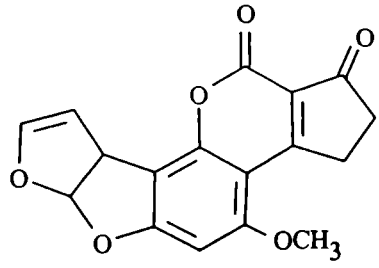
d. 

e. 

f. 

g. 

Ascorbic acid

h. 

Aflatoxin B_1

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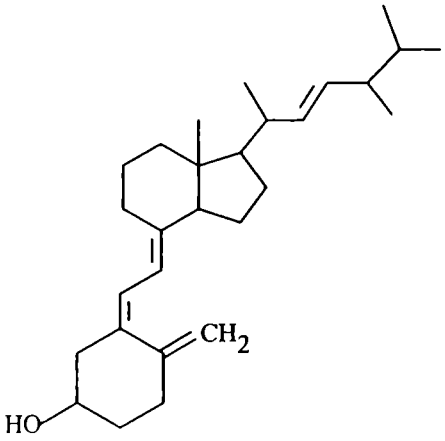
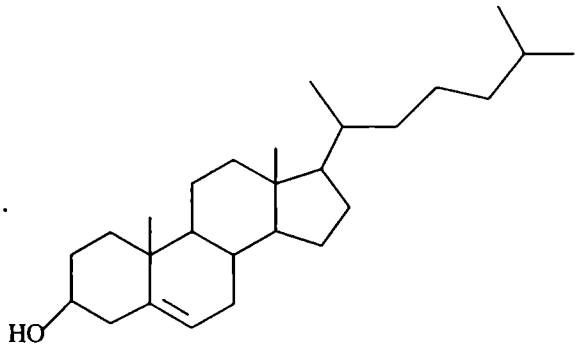
i.



Vitamine D_2

j.



Cholesterol

11. List the following atoms or groups in order of increasing priority:

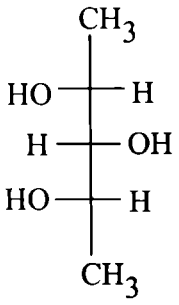
a. $-OC_2H_5$, $-OCH_3$, -COOH, -OH

b. -F, -OH, -COOH, -H

c. $-C^*$ abc (S), - C^* abc (R), -OH, -H

12. Which of the following compounds exhibit optical activity:

a.



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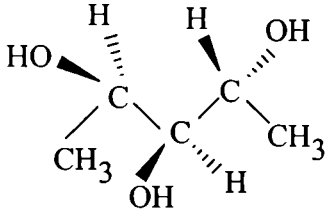

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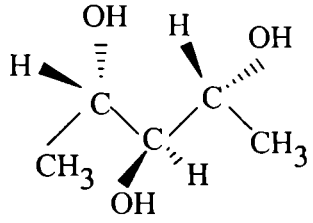

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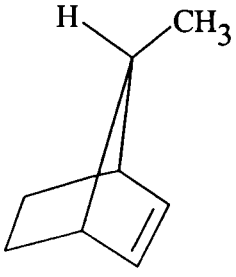

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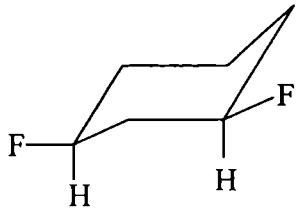

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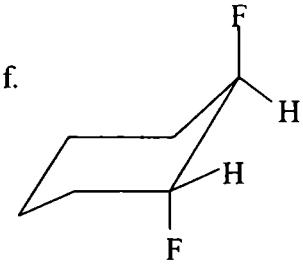

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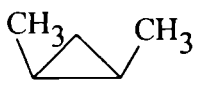
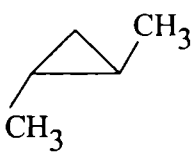
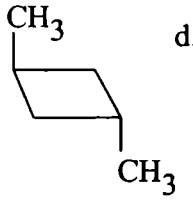
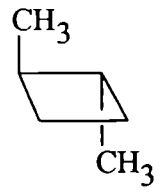
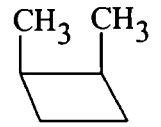
13. Which of the following substituted cycloalkanes exhibit optical activity:

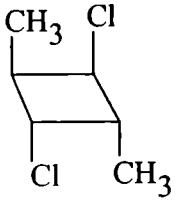
a. 

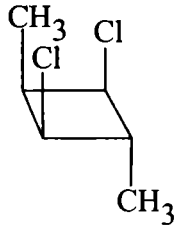
b. 

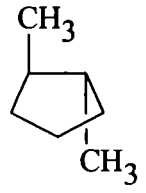
c. 

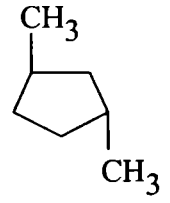
d. 

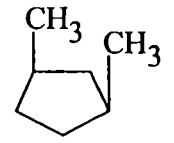
e. 

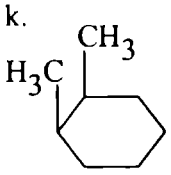
f. 

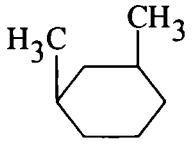
g. 

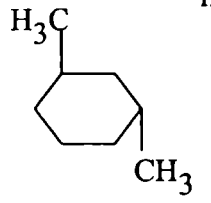
h. 

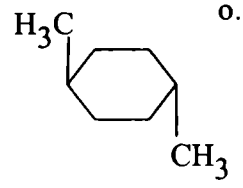
i. 

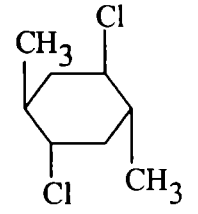
j. 

k. 

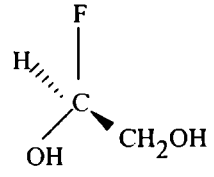
l. 

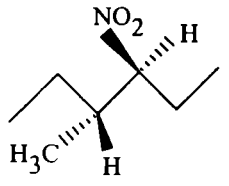
m. 

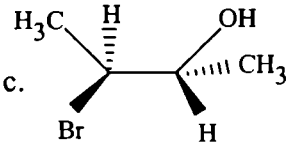
n. 

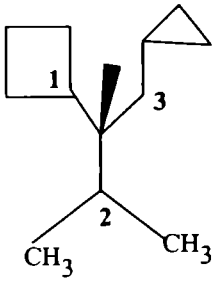
o. 

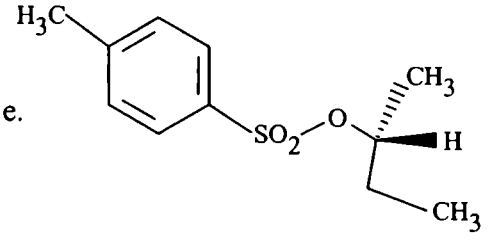
14. Assign (R) and (S) configuration for the following substances:

a. 

b. 

c. 

d. 

e. 

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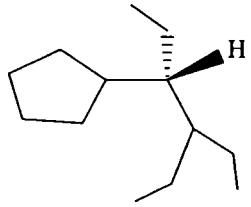
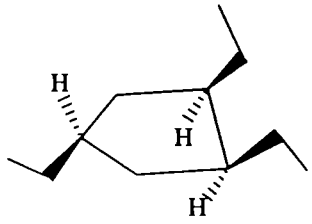
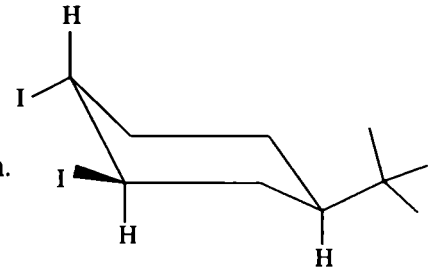
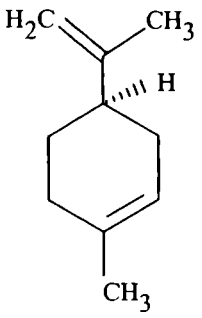
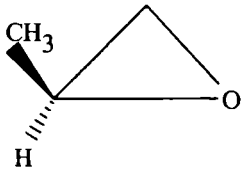
f. 

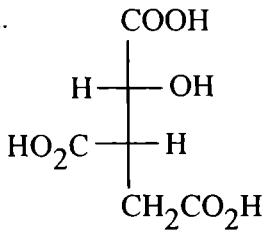
g. 

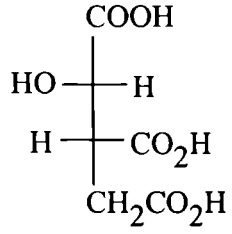
h. 

i. 

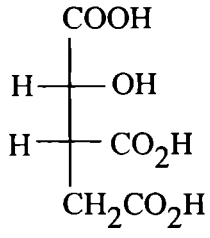
j. 

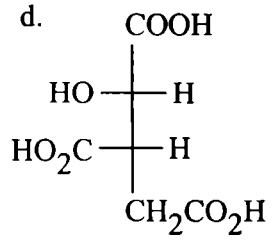
15. Assign configuration, using the sequence rule, to each chiral center for the stereoisomeric isocitric acids and alloisocitric acids:

a. 

b. 

isocitric acids

c. 

d. 

alloisocitric acids

16. Draw structural formulas for each of the following compounds, clearly showing stereochemistry:
    a. (R)-4-methyl-4-phenyl-2-cyclohexenone
    b. Methyl (1S)-cyano- (2R)-phenylcyclopropanecarboxylate
    c. L-erithro-2- (methylamino)-1-phenylpropan-1-ol [(-) ephedrine]
    d. (7R, 8S)-7,8-epoxy-2-methyloctadecane (the sex attractant of the female gypsy moth)
    e. an achiral isomer of 1,2-dimethylcyclohexane
    f. a chiral isomer of 1,2-dibromocyclobutane
    g. two achiral isomers of 3,4,5-trimethylheptane

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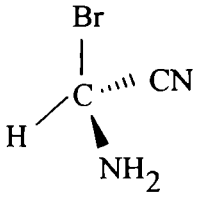
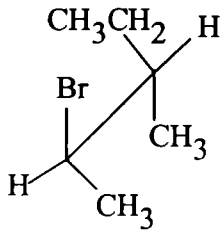
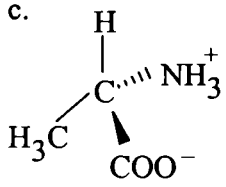
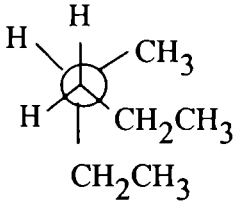
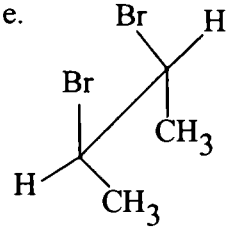
17. Draw at least three Fisher projections for each of the following compounds:

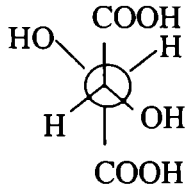
a. 

b. 

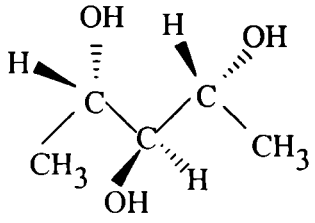
c. 

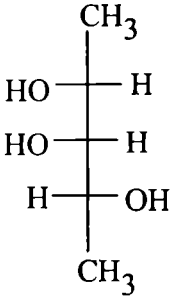
d. 

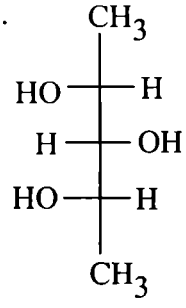
e. 

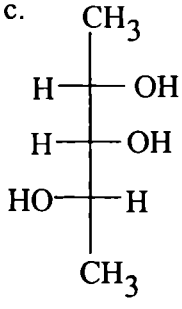
f. 

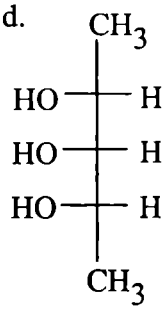
18. Which of Fisher projection correctly depicts the following compound:



a. 

b. 

c. 

d. 

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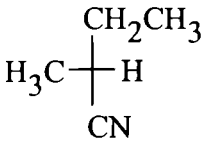
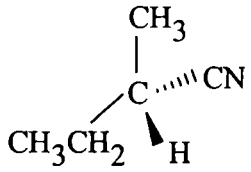
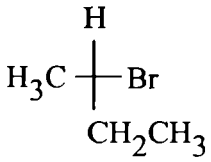
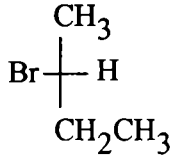
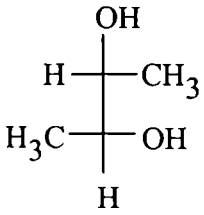
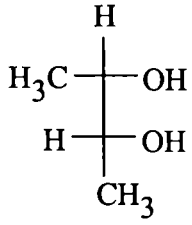
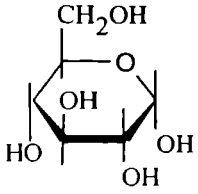
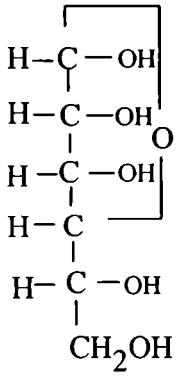
19. The following pairs of compounds are related as enantiomers, diastereoisomers, epimers, identical compounds:

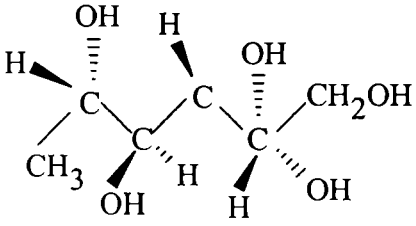
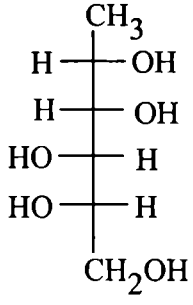
a.  and 

b.  and 

c.  and 

d  and 

20. The following stereoisomers are related as:

a) enantiomers

b) diastereoisomers

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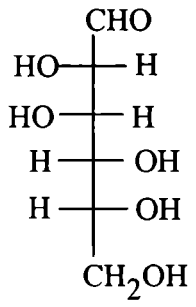
c) epimers

d) identical compounds

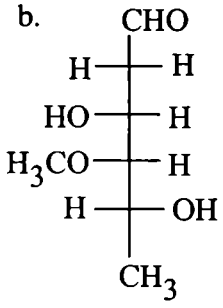
21. Draw clear conformational representation of the β-pyranose forms of each of the following carbohydrates:

a.



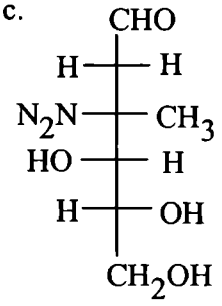
D-mannose

b.



D-chromose A

c.



D-vancosamine

22. Draw the following stereoisomers. Which of them should be more stable? Explain.

a. α or β-D-fructofuranose

b. α or β-D-manopyranose

c. *cis* or *trans* - decalin

d. *cis* or *trans* –1,3-dibromocyclohexane

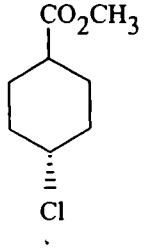
23. Draw the most stable conformers of:

a. N-methyl-piperidine

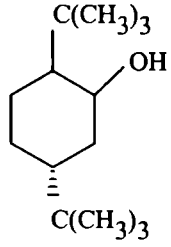
b. erithro 2-amino-3-hydroxi-aminobutane

c. *cis*-1-ethyl-2-methylcyclohexane

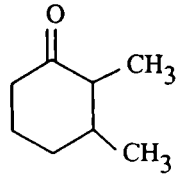
d.



e.



f.



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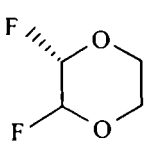
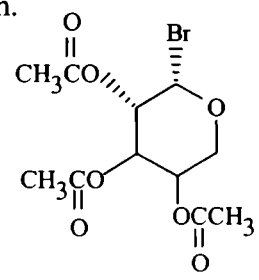
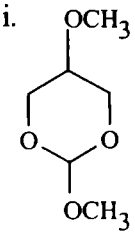
g. 

h. 

i. 

24. Draw the two chair conformations for each of the stereoisomers of trans-1-*tert*-buthyl-3-methylcyclohexane. For each pair, indicate which conformation is more stable.

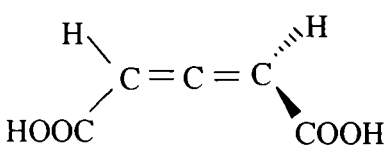
25. Which of the following object are chiral?

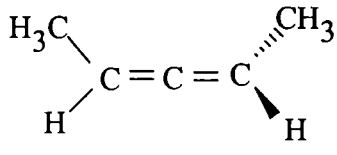
a. a mug
b. a mug with DAD written on one side
c. a mug with MOM written on one side
d. a mug with DAD written opposite the handle
e. a mug with MOM written opposite the handle
f. a coffee pot

26. Give examples witch exhibit optical activity for:

a. a spirane
b. an ansa compound
c. a catenane
d. a paracyclophane
e. a helical compound

27. Name and assign (R) and (S) convention for the following chiral compounds lacking asymetric atoms:

a. 

b. 

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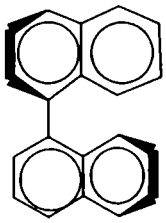
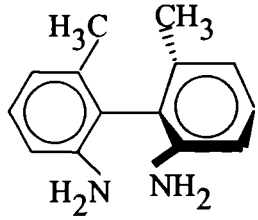
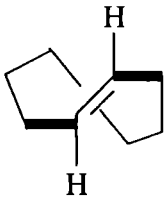
c.



d.



e.



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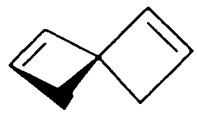
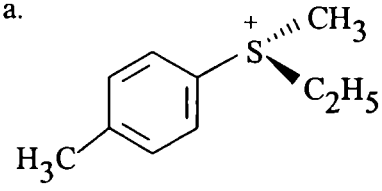


28. How many stereoisomers can present the following substituted derivates of biphenyl? Which of these exhibit optical activity?

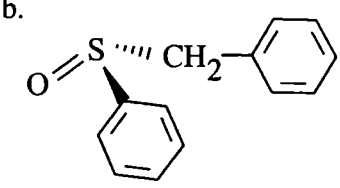
	2	2'	6	6'
a.	A	B	-	-
b.	B	A	-	A
c.	B	A	B	A
d.	A	A	B	B

29. Assign (R) and (S) convention for the following compounds with stereogenic centers at sulfur and phosphorus:

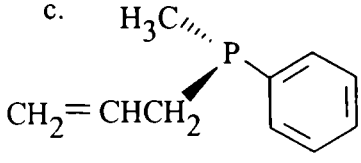
a.



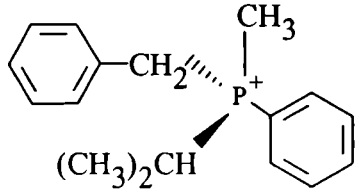
b.



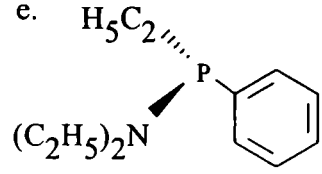
c.



d.



e.



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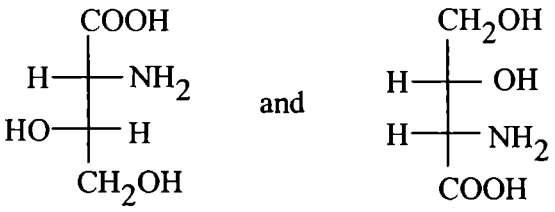
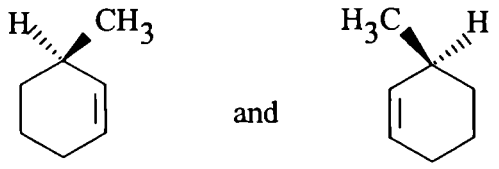
30. Indicate whether the relationship in each of the following pairs of compounds is identical, enantiomeric, or diastereomeric:

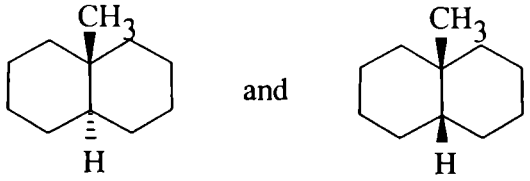
a.



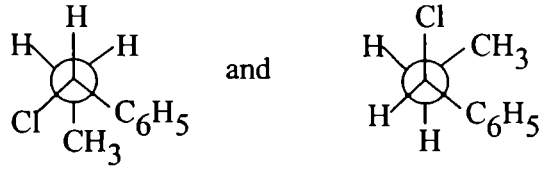
b.



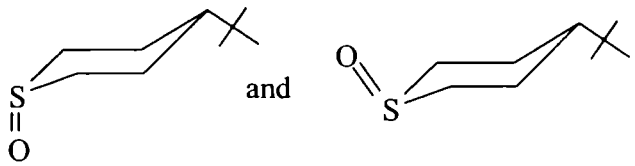
c.



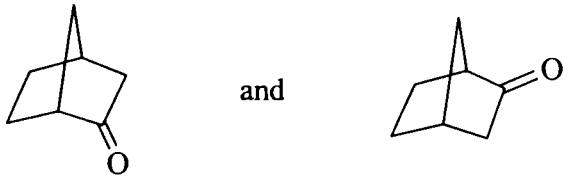
d.



e.



f.



31. An amino acid having the constitution shown below has been isolated from horse chestnuts. It is configurationally related to L-proline and has the R configuration at C-3. Write a stereochemically correct representation for this compound.

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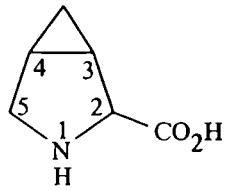
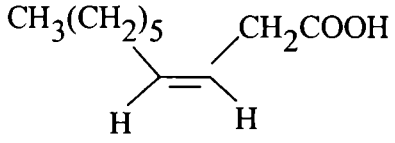
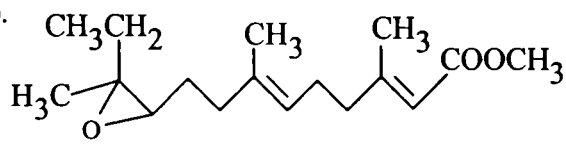


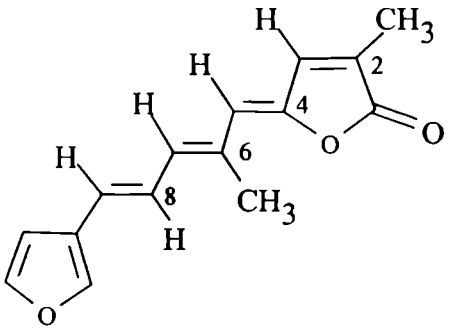
horse-chestnut amino acid

32. One of the diastereomers of 2,6-dimethylcyclohexyl benzyl ether exhibits two doublets for the benzylic protons in its NMR spectrum. Deduce the stereochemistry of this isomer.

33. Name according to the sequence rule the following molecules with double-bond geometry:

a. 

b. 

c. 

34. Draw structural formulas for each of the following compounds, clearly showing stereochemistry:

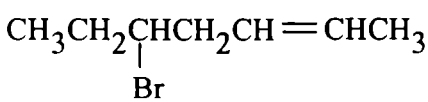
a. (E)-3,7-dimethyl-2,6-octadien-1-ol

b. 2,6-dimethyl-2Z,4E,6E-octatriene

c. (Z)-2-methyl-2-butenol

d. (11Z, 13Z)-hexadecadienal

35. Name and draw the stereoisomers for the following compound:



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36. Which of the following compounds have a stereoisomer that is a meso compound?

a. 1,4-dimethylcyclohexane

b. 1-bromo-2-methylcyclohexane

c. 1,3-dimethylcyclohexane

d. 1,2-dichlorocyclobutane

e. 2,4-dibromopentane

f. 2,5-dibromohexane

37. Which of the following compounds have a stereoisomer that is achiral?

a. 2,3-dibromobutane

b. 2,3-dichloropentane

c. 2,4-dichloropentane

d. 1,2-dimethylcyclobutane

e. 1-bromo-4-methylcyclohexane

38. a. Draw the nine configurational isomers of 1,2,3,4,5,6-hexachlorocyclohexane.

b. From the nine configurational isomers, identify one pair of enantiomers

c. Draw the most stable conformation of the most stable configurational isomer.

39. What is the absolute configuration of:

a. (-)-glyceric acid

b. (+)-isoserine

c. (-)glyceraldehyde

40. (S)-(-)-2-Methyl-1-butanol can be oxidized to (+)-2-methylbutanoic acid without breaking any of the bond to the chirality center. What is the configuration of (-)-2-methylbutanoic acid?

41. When (S)-(+)-1-chloro-2-methylbutane reacts with chlorine, one of the products formed is (-)-1,4-dichloro-2-methylbutane. Does this product have the R or S configuration?

42. Tell whether the H_a and H_b hydrogens in each of the following compounds are homotopic, enantiotopic, or diastereotopic.

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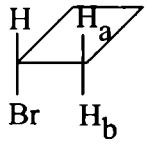
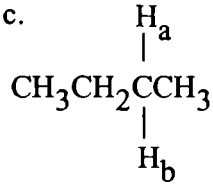
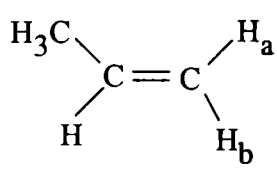
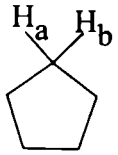
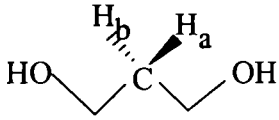
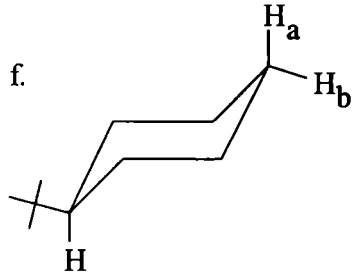
a. 

c. 

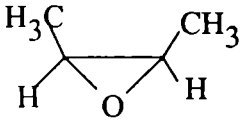
e. 

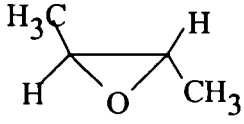
b. 

d. 

f. 

43. Some of the compounds shown contain diastereotopic atoms or groups. Which possess this characteristic? For those that do, indicate the atoms or groups that are diastereotopic and indicate which atom or group is *pro-R* and which is *pro-S*.

a. 

b. 

c. $C_6H_5CHCO_2CH(CH_3)_2$ (OCH$_3$ on the CH)

d. $BrCH_2CH(OC_2H_5)_2$

44. Would you expect to find separable stereoisomers in:

a. 1,4-dichlorocyclohexane

b. chlorocyclohexane (axial or equatorial)

c. 1,2-dimethylcyclopropane

d. N,2-dimethylethylene imine

e. $H_3C-CH(C_3H_7)-C_2H_5$

f. $H_3C-N(C_3H_7)-C_2H_5$

45. The enantiomers of 1,2-dimethylaziridine can be separated even though one of the "groups" attached to nitrogen is a pair of nonbonding electrons. Explain.

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46. Two stereoisomers are obtained from the reaction of HBr with (3S, 4S)-4-bromo-3-methyl-1-pentene. One of the stereoisomers is optically active, and the other is not. Give the structures of the stereoisomers, indicating their absolute configurations, and explain the difference in optical properties.

47. Give the product(s) that would be obtain from the reaction of *cis*-2-butene with each of the following reagents. If the products can exist as stereoisomers, determine the stereochemical relationship:

a. Br_2 in CH_2Cl_2

b. MnO_4^-/HO^-

c. HOBr

d. BH_3 followed by H_2O_2/HO^-

48. Give the product(s) that would be obtain from the reaction of *trans*-2-butene with each of the following reagents. If the products can exist as stereoisomers, determine the stereochemical relationship:

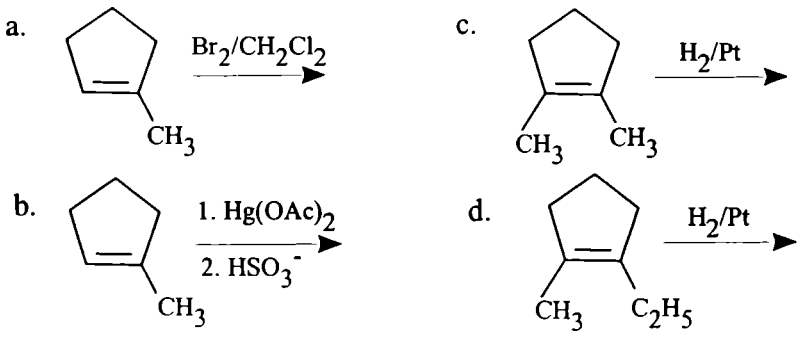
a. Br_2 in CH_2Cl_2

b. MnO_4^-/HO^-

c. HOBr

d. BH_3 followed by H_2O_2/HO^-

49. Give the configuration of the products obtained from the following reactions:



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50. Give the product(s) described for each reaction. Specify all aspects of stereochemistry.

a. stereospecific *anti* addition of bromine to Z- znd E-cinnamic acid

b. solvolysis of (S)-3-bromooctane in methanol

c. stereospecific *syn* elimination of acetic acid from (R,S)-1,2-diphenylpropylacetate

d. stereoselective epoxidation of bicyclo[2.2.1]hept-2-ene proceeding 94% from *exo* direction

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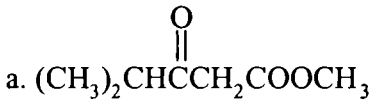
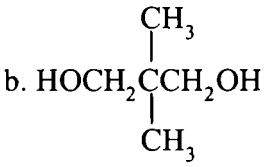
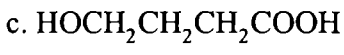
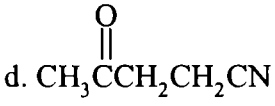
DIFUNCTIONAL COMPOUNDS

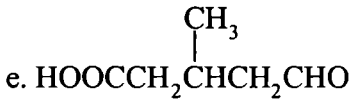
1. Name the following compounds:

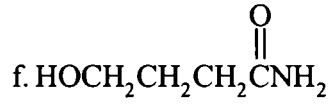
a. 

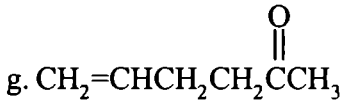
b. 

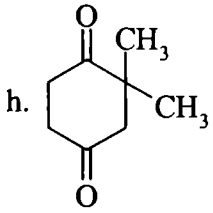
c. 

d. 

e. 

f. 

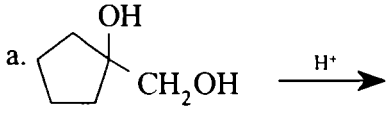
g. 

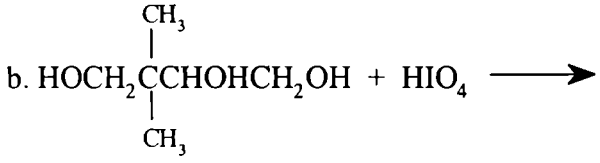
h. 

2. The following names are a mixture of trivial, common, and IUPAC nomenclature. Which is which? Write a structure for each name.

a. β-hydroxyvalerianic acid
b. methyl lactate
c. tetramethylene glycol
d. 3-hydroxypentanoic acid
e. pinacol
f. ethyl benzilate
g. β-ketocaproic acid
h. 3-oxohexanoic acid
i. benzoin
j. α-methoxyphenylacetic acid
k. γ-valerolactone
l. δ-valerolactone

3. Give the principal product(s) of each of the following reactions:

a. 

b. 

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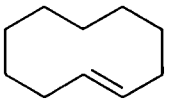
c. $(CH_3)_2CHCHO + HOCH_2CH_2OH \xrightarrow{H^+}$

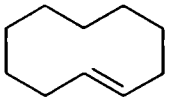
d. $HO(CH_2)_6COOH \xrightarrow{\Delta}$

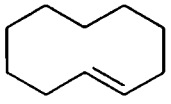
e. $CH_3CH_2CHOHCOOH \xrightarrow{\Delta}$

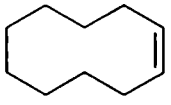
f. $HOCH_2CH_2CH_2COOH \xrightarrow{\Delta}$

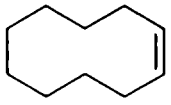
4. For each reaction, what is the stereochemistry of the 1,2-cyclodecanediol produced?

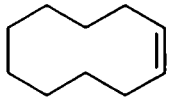
a.  $\xrightarrow{HCO_3H}$ $\xrightarrow[H_2O]{NaOH}$

b.  $\xrightarrow[H_2O_2]{OsO_4}$

c.  $\xrightarrow[H_2O]{Br_2}$ $\xrightarrow[\Delta]{NaOH,\ H_2O}$

d.  $\xrightarrow{HCO_3H}$ $\xrightarrow[H_2O]{NaOH}$

e.  $\xrightarrow[H_2O_2]{OsO_4}$

f.  $\xrightarrow[H_2O]{Br_2}$ $\xrightarrow[\Delta]{NaOH,\ H_2O}$

5. a. Write alternative Lewis structures for periodic acid, $HOIO_3$, and iodic acid, $HOIO_2$, making use of $-O-I^+$ or O=I bonds. Be careful to count electrons and assign formal charges properly; note that iodic acid has a lone pair of electrons on iodine.

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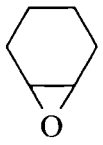
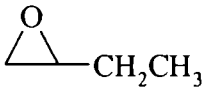
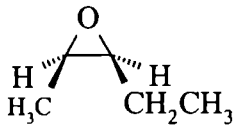
b. *cis*-1,2-Cyclopentanediol is oxidized to glutaraldehyde (1,5-pentanedial) by periodic acid much more rapidly than the trans isomer. Explain.

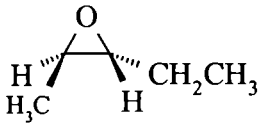
c. Suggest a method whereby periodic acid could be used to distinguish between 1,2,3-pentanetriol and 1,2,4-pentanetriol.

6. What alkene would you treat with a peroxyacid in order to obtain each of the following epoxides?

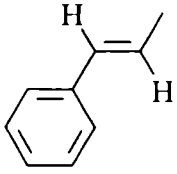
a. 

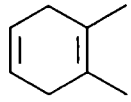
b. 

c. 

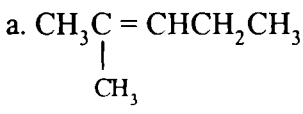
d. 

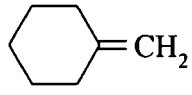
7. Give the major product of the reaction of each of the following compounds with one equivalent of a peroxyacid. Indicate the configuration of the product.

a. 

b. 

8. Give the products that would be formed from the reaction of each of the following alkenes with OsO_4 followed by treatment with H_2O_2.

a. 

b. 

9. What stereoisomers would be formed from the reaction of each of the following alkenes with OsO_4 followed by treatment with H_2O_2?

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a. *trans*-2-butene

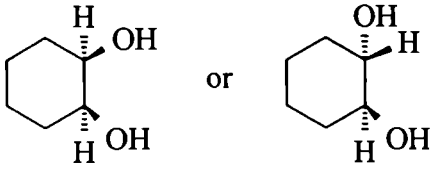
b. *cis*-2-butene

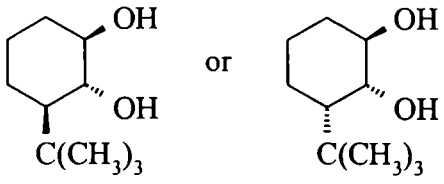
c. *cis*-2-pentene

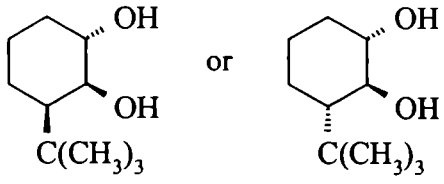
d. *trans*-2-pentene

10. An alkene is treted with OsO_4 followed by H_2O_2. When the resulting diol is treated with HIO_4, the only product obtained is an unsubstituted cyclic ketone with molecular formula $C_6H_{10}O$. What is the structure of the alkene?

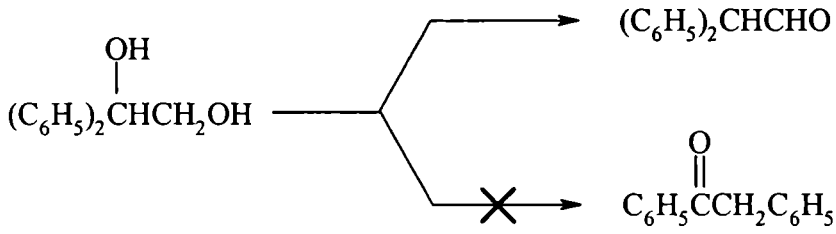
11. Which of each pair of diols is cleaved more rapidly by periodic acid?

a. 

b. 

c. 

12. Pinacol rearrangement of 1,1-diphenyl-1,2-ethanediol gives diphenylacetaldehyde and not phenylacetophenone. Explain.



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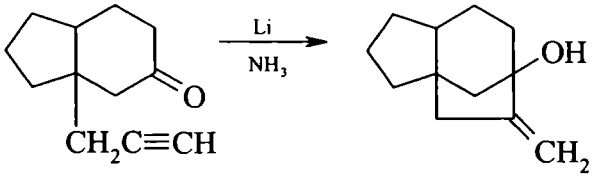
13. Suggest a method whereby one might distinguish *cis*-1,3-cyclohexanediol from *trans*-1,3-cyclohexanediol.

14. *cis*-1,2-Cyclopentanediol reacts with benzaldehyde (C_6H_5CHO) in the presence of HCl and anhydrous magnesium sulfate to give two compounds with the formula $C_{12}H_{14}O_2$. What are the structures of the two compounds? What is the function of magnesium sulfate? Explain why *trans*-1,2-cyclopentanediol does not undergo a similar reaction.

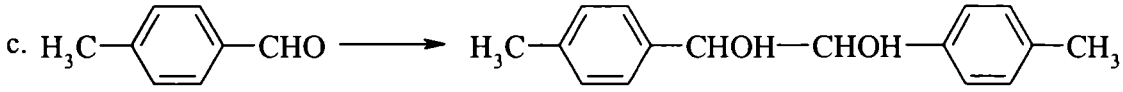
15. The following reaction is similar to the acyloin condensation. Propose a mechanism for the reaction:

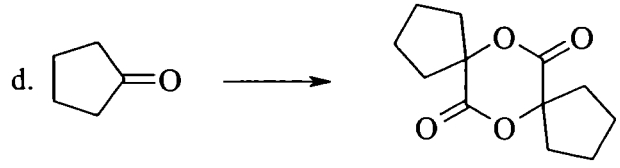


16. Show how one may accomplish each of the following conversions in a practical manner:

a. $CH_3COCH_3 \longrightarrow (CH_3)_3CCOOH$

b. $CH_3CH_2COOH \longrightarrow CH_3CH_2CHOHCH(CH_3)COOH$





e. $CH_3CH_2COOH \longrightarrow CH_3CH_2CHOHCHOHCH_2CH_3$

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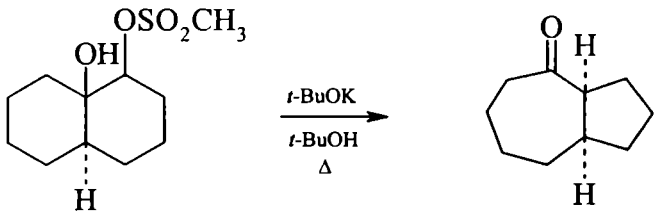
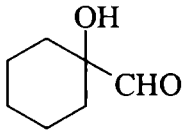
17. Propose a mechanism for the following reaction:



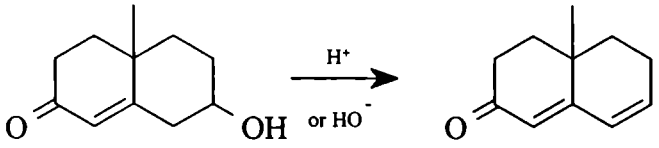
18. Making use of 1,3-dithiane, show how each of the following compounds may be synthesized.

a. 

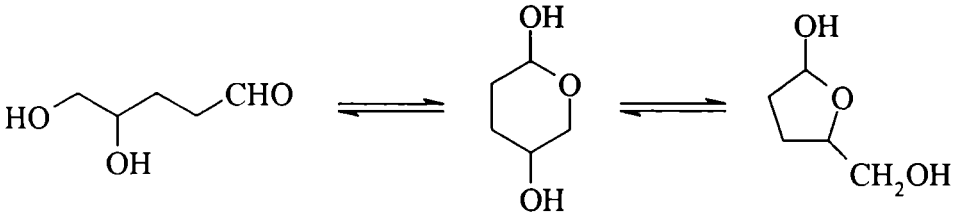
b. $CH_3\overset{\overset{O}{\|}}{C}CH_2CHCH_2CH_3$

c. $CH_3CH_2CH_2\overset{\overset{O}{\|}}{C}CH_2CH_2CH(CH_3)_2$

19. The following dehydration is exceedingly facile. Explain.



20. a. 4,5-Dihydroxyhexanal exists in solution largely as a cyclic hemiacetal. Predict which form will predominate at equilibrium.



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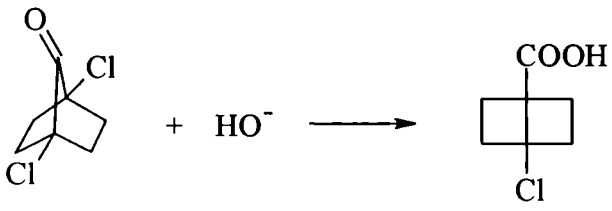
b. When 4,5-dihydroxyhexanal is treated with silver oxide and the resulting dihydroxyhexanoic acid is treated with acid, a lactone results. What is the structure of the lactone?

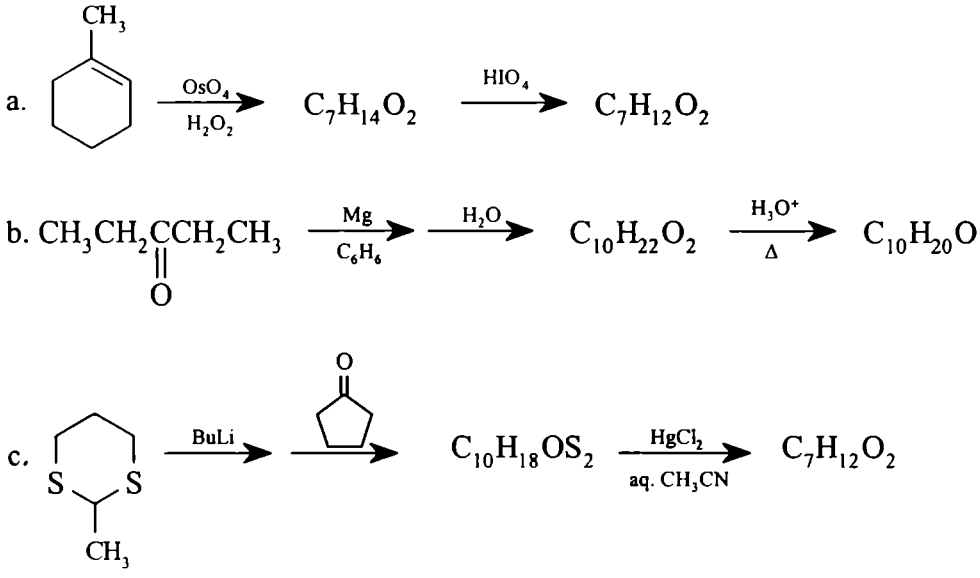
21. a. Propose a mechanism for the following reaction:



b. Name the reactant and the product in the reaction.

22. Explain why *cis*-3-hydroxycyclohexanecarboxylic acid forms a lactone, whereas the *trans* isomer does not. Write a three-dimensional structure for the lactone.

23. Give the expected product for each reaction sequence:



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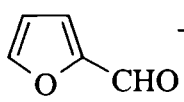
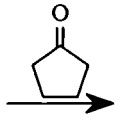
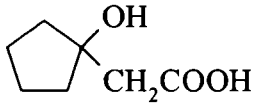
d.  $\xrightarrow[C_2H_5OH]{KCN}$ $C_{10}H_8O_4$ $\xrightarrow{Cu(OAc)_2}$ $C_{10}H_6O_4$ $\xrightarrow[\Delta]{\text{conc. KOH}}$ $\xrightarrow{H_3O^+}$ $C_{10}H_8O$

e. *trans*-2-butene $\xrightarrow{HCO_3H}$ $\xrightarrow[H_2O]{NaOH}$ $C_4H_{10}O_2$  $C_9H_{16}O_2$

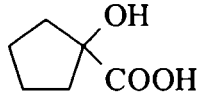
24. Show how each of the following compounds may be synthesized from starting materials containing five or fewer carbons.

a. 

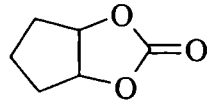
b. $(CH_3)_2CHC(=O)C(=O)CH(CH_3)_2$

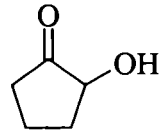
c. $(CH_3)_3CC(=O)CH(OH)CH_2CH_3$

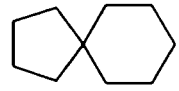
d. $(CH_3CH_2)_3CC(=O)CH_2CH_3$

e. 

f. $(CH_3)_2CHCH_2C(=O)CH_2CH(OH)CH_3$

g. 

h. 

i. 

25. 1-Phenylethane-1-*d*, $C_6H_5CHDCH_3$, **E**, has been prepared in optically active form. This compound is particularly interesting because its asymmetry is due entirely to the isotopic difference between H and D; the magnitude of its rotation has the value of $[\alpha]_D = \pm 0.6°$. The absolute configuration of **E** is related to the known configuration of mandelic acid by the following sequence of reactions:

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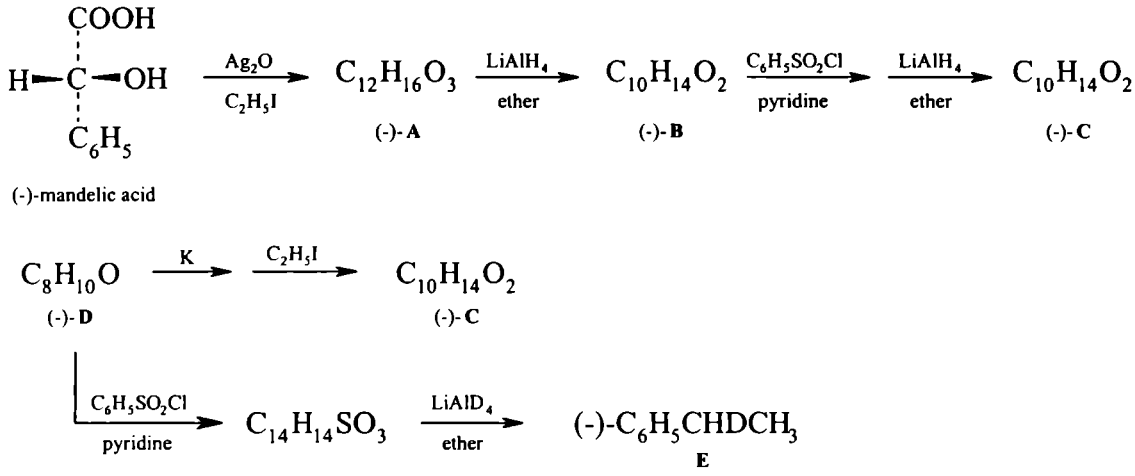

Deduce the absolute configuration of (-)-**E** and the structure and configuration of each intermediate, **A** through **D**, in the sequence. Assign the proper R,S notation to each structure, **A** through

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CARBOHYDRATES

1. Define the terms:
    a. epimer
    b. anomer
    c. diastereomer
    d. monosaccharide
    e. reducing sugar

    Give an example of each.

2. What structural relationship is indicated by the term D-sugar? Why are (+) glucose and (-) arabinose both classified as D-sugars?

3. a. Write Fisher projection for the following sugars: L-fructose, L-arabinose, L-sorbose
    b. How many stereisomers are in each case?

4. Determine which of the following sugar pairs are diastereomers, epimers, enantiomers, or and aldose-ketose pair:
    a. D-arabinose and D-ribose
    b. D-arabinose and L-arabinose
    c. D-arabinose and D-xylose
    d. D-mannose and D-fructose

5. Using Cahn-Ingold-Prelog give the rational name for:
    a. D-glucose
    b. D-fructose
    c. D-ribose
    d. 2-desoxi-D-ribose

6. Draw Haworth structures for the following compounds:
    a. β-D-altropyranose
    b. α-D-glucopyranose

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c. β-D-fructofuranose

d. sucrose

e. β-D-talopyranose

7. Write Fisher projections (open chain and cyclic forms) for the following compounds in solution:

   a. D-glucose

   b. D-galactose

   c. L-sorbose

   d. D-mannose

8. Draw β-D-galactopyranose and β-D- mannopyranose in chair conformations and label all the ring substituents as either axial or ecuatorial. Which would you expect to be more stable?

9. The most stable conformation of most aldopyranose is one in which the largest group – the $-CH_2OH$ group - is equatorial. However, D-idopyranose exists primarily in a conformation with an axial $-CH_2OH$ group. Write formulas for the two chair conformations of α-D-idopyranose (one with the - CH_2OH group axial and one with the - CH_2OH group equatorial) and provide an explanation.

10. a. Which of the following sugars undergo mutarotation: 4-(α-D-glucopyranosyl)-D-glucopyranose, 6-(α-D-galactopyranosyl)-β-D-glucopyranose, 4-(β-D-galactopyranosyl)-D-glucopyranose, β-O-methyl-D-ribofuranose, β-pentaacetyl-D-glucopyranose.

    b. Write the Hawarth formulas for each.

    c. Which of them are reducing sugars?

    d. Which are the reactions that point out the reducing character?

11. If the specific rotation of pure α-D-glucopyranose is $+112.2^{o}$ and the specific rotation of pure β-D-glucopyranose is $+18.7^{o}$, show how the equilibrium percentages of α and β anomers can be calculated from the equilibrium specific rotation of $+52.6^{o}$.

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12. Write the epimarization mechanism of a glucide in basic medium.

13. Although mutarotation of the D-glucopyranoses is catalyzed by either acid or bases, one of the most effective catalyst is 2-hydroxypyridine. Write the mechanism that accounts for this.

14. Ascorbic acid it's a powerful reducing agent, derivate of monosaccharides. It is synthesized by all mamals except for guinea pigs, appes, fruit-eating bats and humans.
    a. Describe the synthesis of ascorbic acid starting with D-glucose.
    b. Give the Haworth formula for it
    c. Write the redox reaction.

15. Ascorbic acid present in solution two acidic groups with $pK_1 = 4.2$ and $pK_2 = 11.6$.
    a. Which are the mobile protons?
    b. Explain the big difference between the pK values.

16. Predict the product (if any) of bromine oxidation of each of the following compounds:
    a. D-erithrose
    b. A glycoside
    c. β-D-ribose
    d. Sucrose

17. Which of the aldohexoses form meso-aldaric acids upon oxidation with hot nitric acid?

18. Name the pairs of aldohexoses that are oxidized to identical aldaric acids.

19. Predict the products (if any) of the periodic acid oxidation of the following compounds:
    a. D-glucose
    b. A tetrulose
    c. Penta-O- acetyl-β-Dglucopyranose
    d. Arabinoside

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20. Draw structures for furanose and pyranose forms of D-ribose. Show how you could use periodate oxidation to distinguish between a methyl ribofuranoside and a methyl ribopyranoside.

21. There are two uronic acids that can be obtained from D-fructose. Write their structures. (Fisher and Haworth formulas).

22. It is known that ketoses dosen't react with Fehling reagent. There are two acids that can be obtained from D-fructose with Fehling reagent. Explain and write the structures of the acids.

23. How many lactones can be formed upon oxidation of glucose?

24. Heating D-altrose with dilute acid produces a nonreducing anhydro sugar, $C_6H_{10}O_5$. Methylation of the anhydro sugar followed by acid hydrolysis yields 2,3,4-tri-O-methyl-D-altrose. The formation of the anhydro sugar takes place through a chair conformation of β-D-altropyranose in which the - CH_2OH group is axial. What is the structure of the anhydro sugar and how is it formed?

25. Show how Emil Fisher proved the configuration of glucose?

26. Which of the aldopentoses form meso-alditols upon reduction with hydrogen and catalyst or a metal hydride? Write the structures of the alditols.

27. What other monosaccharide is reduced only to the aditol obtained from the reduction of:
    a. D-talose
    b. D-galactose

28. What monosaccharide is reduced to two alditols, one of which is the alditol obtained from the reduction of:
    a. D-talose
    b. D-mannose

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29. Which are the aldohexoses that give the same osazone? Draw the structures of the osazones.

30. What two aldoses would yield the same phenylosazone as L-sorbose?

31. Psicose and tagose are two 2-ketohexoses. D-psicose yields the same phenylosazone as D-allose (or D-altrose); D-tagose yields the same osazone as D-galactose (or talose). What are the structures of D-psicose and D-tagose?

32. Indicate the main products (Haworth formulas) for the following reactions:

a. D-mannose + $(CH_3)_2CHOH \xrightarrow{H^+}$

b. D-fructose + $CH_3OH \xrightarrow{H^+}$

c. β-O-Methyl-D-arabinofuranoside $\xrightarrow[t^o]{H_2O/H^+}$

d. D-glucose + $(CH_3)_2SO_4 \xrightarrow{NaOH}$

e. α–D-galactopyranose + $(CH_3)_2CO \xrightarrow{H^+}$

f. β-O-methyl-D-galactopyranoside + $C_6H_5CHO \xrightarrow{H^+}$

g. α–D-ribofuranose + $(C_6H_5)_3CCl \longrightarrow$

h. β-pentaacetyl-D-glucopyranose + HBr $\longrightarrow$

33. **A**, **B**, and **C** are three aldohexoses. **A** and **B** yield the same optically active alditol when thet are reduced with hydrogen and catalyst; **A** and **B** yield different phenylosazones when treated with phenylhydrazine. **B** and **C** give the same phenylosazone but different alditols. Assuming that all are D-sugars, give names and structuresfor **A**, **B** and **C**.

34. Aldohexoses **A** and **B** form the same osazone. **A** is oxidized by nitric acid to an optivally active aldaric acid and **B** is oxidized to an optically inactive aldaric acid. Ruff degradation of either **A** or **B** forms aldopentose **C**, which is oxidized by nitric acid to an optically active aldaric acid. Ruff degradation of **C** forms **D**, which is oxidized by nitric acid to an optically active aldaric acid. Ruff degradation of **D** forms (+)-glyceraldehyde. Idenify **A, B, C** and **D.**

35. Write the structures of β-maltose and β-cellobiose and explain which of them should be more stable.

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36. Gentiobiose is a rare disaccharide found in saffron and gentian. It is a reducing sugar and forms only glucose on hydrolysis with aquaous acid. If gentiobiose contains a 1,6'-β-glycoside link, hat is its structure?

37. Trehalose is a nonreducing disaccharide found in the blood of insects. Upon hydrolysis, only D-glucose is obtained. What are the possible structures of trehalose? If trehalose is hydrolysed only by α-glycosidase, which structure is correct?

38. Isotrehalose and neotrehalose are chemically similar to trehalose, except that neotrehalose is hydrolysed only by β-glycosidases whereas isotrehalose is hydrolysed by both α- and β-glycosidases. What are the structures of isotrehalose and neotrehalose? Are they also reducing sugars?

39. In contrast to amino acids in protein which can only interconect in one way the monosaccharide units in oligosaccharide and polisaccharide can attach to one another at multiple points. Two identical monosaccharides can bond to form 11 different disaccharides, whereas, two identical amino acids can make only one dipeptide. Without naming them, how many of the 11 disaccharides formed between two glucoses can you describe?

40. Bleomycin is an antibiotic active against squamous cell carcinomas. Part of the structure of this compound is a reducing disaccharide. If it's hydrolysed in acidic solution yields to D-mannose and L-gulose. The hydrolysis is also catalysed by enzymes specific for α-mannose glycosides. If is treated with excess dimethylsulfat and then acidic hydrolysis yields to 2,3,4,6-tetramethyl ether of D-mannose and 3,4,6-trimethyl ether of L-gulose. What is the structure of the disaccharide?

41. Linustatin ($C_{16}H_{27}NO_{11}$) is a discccharide in defatted meal, that can protect livestock against the toxic effects of selenium compounds in forage plants. Acidic hydrolysis of linustatin yields D-glucose as the only monosaccharide. Enzymatic hydrolysis with β-glucozidase yields two compounds: D-glucose and a glycoside. Comparison of the ^{13}C NMr spectrum of linustatin indicates the presence of to CH_3 groups, one quaternary C, and one substituted

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CH_2OH group, as well as other carbon atoms. The IR spectrum of linustatin shows strong absorpstion at 3440cm^{-1} and weak absorption at 2240 cm^{-1}. No carbonyl absorption is apparent. What is the structure of linustatin?

42. Raffinose is a trisaccharide found in beets. Complete hydrolysis of raffinose yields D-fructose, D-glucose, and D-galactose. Partial enzymatic hydrolysis of raffinose with invertase yields D-fructose and the disaccharide melibiose. Partial hydrolysis of raffinose with an α-glycosidase yields D-galactose and sucrose. Methylation of raffinose followed by hydrolysis yiels 2,3,4,6-tetra-O-methylgalactose; 2,3,4-tri-O-methylglucose; and 1,3,4,6-tetra-O-methylfructose. What are the structures of raffinose and melibiose? Is raffinose a reducing or nonreducing sugar? Is raffinose capable of mutarotation?

43. Alginic acid, isolated from seeweed and used as a thickening agent for ice cream and other foods, is a polymer of D-mannuronic acid with β(1,4) glycosidic linkages.
    a. Draw the structure of alginic acid.
    b. What is the maximum number of stereoisomers for mannuronic acid?

44. Pectic acid is a structural polysaccharide of D-galacturonic acid, in pyranosic form, with α(1,4) glycosidic linkages. Draw the structure of pectic acid.

45. Heparin is a glycosaminoglycan found in mast cells. Is used in medicine as an anticoagilant. It has equal proportions of D-glucuronic acid and D-glucosamine, in pyranosic forms, with α(1,4) glycosidic linkages; the hydroxyl group at C_2 in D-glucuronic acid residues is a sulphuric ester; SO_3H groups have been identified at N atoms and hydroxyl groups at C_6 , in D-glucosamine residues.
    Draw the disaccharide repeating unit in heparin (Haworth structure).

46. Hyaluronic acid is most abundant GAG in the vitreous humor of the eye and the synovial fluid of joints.
    Write the Haworth structure of hyaluronic acid knowing the following:
    a. Enzymatic hydrolysis yields N-acetylglucosamine and D-glucuronic acid, in equal proportions.

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b. The two residues are in pyranosic forms, linked by β(1,4) and β(1,3) glycosidic bonds.

47. Chitin is a structural polysaccharide of the arthropods (crabs and insects). Chitin is a liniar polysaccharide consisting of β(1,4) linked N-acetyl-D-glucosamine. Upon hydrolysis, chitin yields 2-amino-2-deoxy-D-glucose. Draw the Haworth structure for chitin, knowing that the residues are in pyranosic forms.

48. What structural differences characterize starch, cellulose, and glycogen?

49. Predict the major product (and give a structure or partial structure) when cellulose is treated with:
    a. an exces of hot aqueous H_2SO_4, then water.
    b. hot water
    c. hot aqueous NaOH solution
    d. an exces of NaOH and dimethyl sulfate

50. Name an example of each of the following classes of compounds:
    a. glycoprotein
    b. proteoglycan
    c. disaccharide
    d. glycosaminoglycan

51. Give one function of each of the following:
    a. glycogen
    b. glycosaminoglycans
    c. glycoconjugates
    d. proteoglycans
    e. glycoproteins
    f. polysaccharides

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52. Compare the structures of proteoglycan and glycoproteins. How are structural differences related to their function?

53. What is the difference between a heteropolysaccharide and a homopolysaccharide? Give examples.

54. In glycoproteins, what are the three amino acids to which the carbohydrate groups are most frequently linked?

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AMINO ACIDS

1. Give a classification of amino acids.

2. Which amino acid has a hidrophobic side chain: Ile, Asp, Thr, Gly, Gln?

3. Give the structure and rational nomenclature for the following amino acids: leucine, serine, aspartic acid, methionine, arginine.

4. Define the following terms:
   a. α-carbon
   b. isoelectric point
   c. hydrophobic amino acid
   d. peptide bond
   e. essential amino acid

5. Show how the isoelectric point of an amino acid can be computed from pK_1 and pK_2.

6. Arginine has the following pK_a values: $pK_1 = 2.17$, $pK_2 = 9.04$ and $pK_R = 12.48$
   a. What is the structure and net charge of arginine at the following pH values? 1, 5,10, 12.
   b. Calculate the isoelectric point.
   c. Write the resonance structure, to show the stability of protonated guanidino group.

7. Glutamic acid has the following pK_a values $pK_1 = 2.19$, $pK_2 = 9.67$ and $pK_R = 4.25$
   a. Draw the structure of the amino acid as the pH of the solution changes from highly acidic to strongly basic.
   b. Calculate the isoelectric point
   c. In what direction does the amino acid move when placed in an electric field at the following pH values: 2, 7, 12.
   d. Sketch the titration curve for the amino acid.

8. Monosodic glutamate is used as aroma in food industry. Write the structure for this compound.

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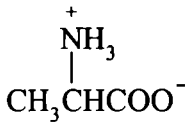
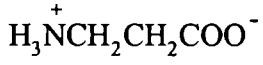
9. Lysine has three ionizable functional groups.
   a. Write the equilibrium equations for its three ionizations and assign the proper pK_a for each. Draw the structure of lysine in each ionization state.
   b. Draw the structure of lysine at the following pH values: 1, 4, 10, 12. What is the net charge on these pH values?

10. The pK_a for β-alanine and γ-amino-n-butyric acid are shown below. Compare these values with the pK_as for the α-alanine and explain the difference.



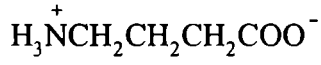
α-alanine

$pK_1 = 2.35$
$pK_2 = 9.87$



β-alanine

$pK_1 = 3.55$
$pK_2 = 10.24$



γ-aminobutyric acid

$pK_1 = 4.03$
$pK_2 = 10.56$

What are the isoelectric points for the three amino acids?

11. For each of the following compounds write the structure of the principal ionic species presenting in aqueous solution at pH 2, 7, and 12:
   a. isoleucine
   b. aspartic acid
   c. glycylglycine (gly-gly)
   d. lysylglycine (lys-gly)

12. A mixture containing aspartic acid ($pH_i = 2.77$), arginine ($pH_i = 10.76$) and serine ($pH_i = 5.7$) is separated by electrophoresis. Explain the separation (pH).

13. L-amino acids have the S configuration at the alpha carbon. Cystein is the only acid that has R configuration. Explain.

14. Threonine is α-amino-β-hydroxibutiric acid. Determine:
   a. The number and the structures for the configurational isomers.
   b. For the treo isomer from the L family give the posible conformational isomer.

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15. In proteins most amino acids have S configuration. In nature are also amino acids with R configuration. Write the projection formulas for:
    a. R – valine
    b. R – leucine

16. Describe the differences between His and Pro with respect to the size, shape, and polarity of their side chain.

17. Using Gabriel method write the chemical reactions for sinthesis of:
    a. glycine
    b. alanine
    c. glutaric acid
    d. phenylalanine

18. Using Strecker method write the chemical reactions to obtain:
    a. glycine
    b. alanine
    c. phenylalanine

19. Obtain the following amino acids using as starting material acetilaminomalonic ester;
    a. alanine
    b. phenylalanine
    c. glutamic acid
    d. serine

20. β-Amino acids are obtained through Hoffman degradation. Write the reaction for synthesis of: *o*-aminobenzoic acid and β-alanine.

21. Propose syntheses for the following amino acids that do not occur in nature:

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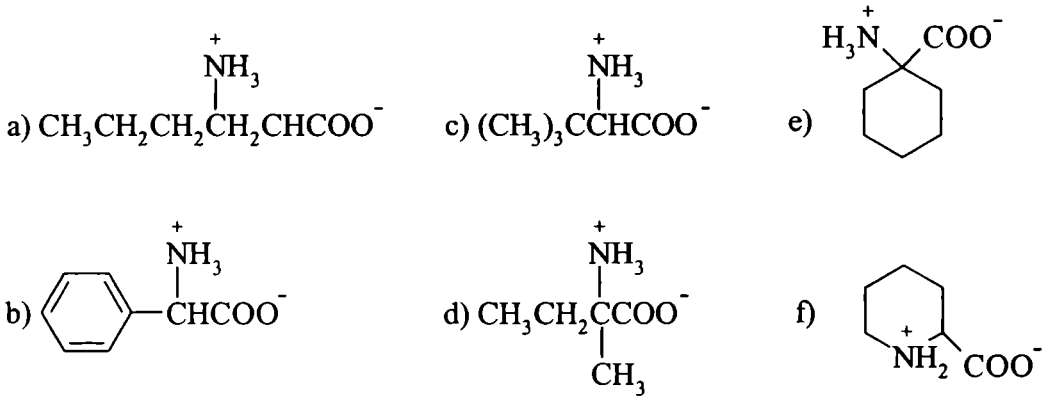
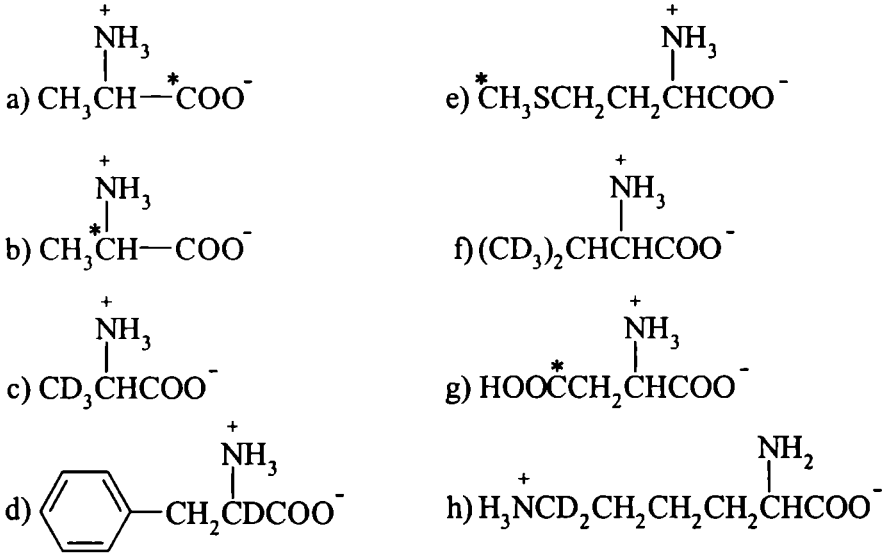
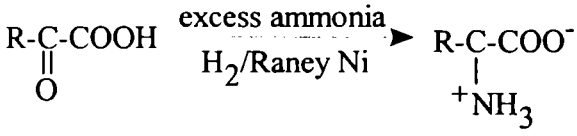


22. The following isotopically labeled amino acids are desired for biochemical research. Show how each may be prepared. The only accepted sources of ^{14}C are $Ba^{14}CO_3$ and $Na^{14}CN$. The ^{14}C-labeled atom is marked with an asterisk in each case. Deuterated compounds may be prepared using D_2O, $LiAlD_4$, or D_2.



23. Amino acids can be synthesised by reductive amination of α-keto-acids:



Biological organism can also convert α-keto-acids into amino acids but, because H_2 and metal catalysts are not avaible to the cell, they do so by different mechanism.

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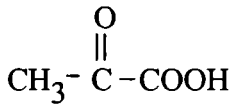
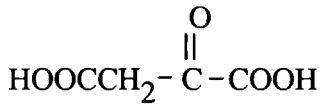
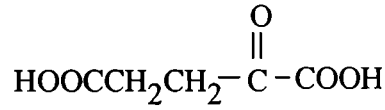
a. What amino acid is obtained from the reductive amination of each of the following metabolic intermediates in the cell?



pyruvic acid



oxaloacetic acid



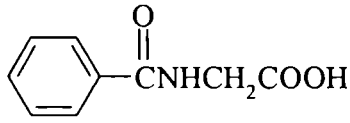
α-ketoglutaric acid

b. What amino acids are obtained from the same metabolic intermediates when they are synthesized in the laboratory?

24. Most amino acids appear blue when treated with ninhydrin reagent. Proline and hydroxiproline appear yellow. Suggest a reason for the difference.

25. Describe the α-amino protecting groups for amino acids and write the reactions of their deprotection.

26. Explain why the benzoyl group cannot be used as a N-protecting group for peptide synthesis, for example N-benzoylglycine.



N-benzoylglycine

27. Glycine undergoes acid-catalyzed esterification more slowly than does propionic acid. Explain.

28. Explain how a benzylester of an amino acid can be deprotected. Write the reaction.

29. Write the products obtained from the reaction of alanine with the following reagents:

a. HCl; b. $NaNO_2$; c. $ClCH_2CN/(C_2H_5)_3N$; d. C_2H_5OH/HCl

e. PCl_5; f. CH_3I/HO^-; g.1-fluoro-2,4-dinitrobenzene; h. NaOH

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30. Write the products obtained from the reaction of valine with the following reagents:

    a. 9-flurenylmethyl chlorocarbonate

    b. N-ethyloxycarbonylphtalimide / Na_2CO_3

    c. Benzyl chlorocarbonate / HO^-

    d. Phenyl isothiocyanate

    e. di-*t*-butyl pyrocarbonate

    f. p-toluensulphonyl chloride

    g. Cu^{2+}

31. Write the reactions for the following trasformations:

    a. ornithine ⟶ arginine

    b. ornithine ⟶ δ– lactam

    c. lysine ⟶ cadaverine

    d. glutamic acid ⟶ pyroglutamic acid

32. Most amino acids are degraded in the liver. This is not true of the branched chain amino acids. Where are they primarily degraded?

33. What are the seven metabolic products produced by the degradation of amino acids?

34. Indicate which of the following amino acids are ketogenic and which are glucogenic:

    a. Tyrosine

    b. Lysine

    c. Glycine

    d. Alanine

    e. Valine

    f. Threonine

35. Some amino acids are classified as both ketogenic and glucogenic. Review the amino acid catabolic pathways and determine which amino acids belong to both categories.

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36. List ten nonessential amino acids in humans. Arginine is classified as an essential amino acid in children even though it is part of the urea cycle. Explain.

37. Most amino acids can be readily interconverted with the corresponding α-keto-acid. This is not true of lysine. When lysine is deaminated, a Schiff base is produced. Explain how this product is formed.

38. Using reaction equations, illustrate how α-ketoglutarate is converted to glutamate. Name the enzymes and cofactors required.

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PEPTIDES AND PROTEINS

1. Distinguish between proteins, peptides and polypeptides.

2. Differentiate the terms in each pair bellow:
   a. globular and fibrous proteins
   b. simple and conjugated proteins
   c. apoprotein and holoprotein

3. Outline the steps to isolate typical protein. What is achieved at each step?

4. Describe the methodes used to purify a protein. What criteria are used to evaluate purity?

5. Name the functions of proteins in the body. What roles do globular proteins play in the living organism?

6. Denaturation is the loss of protein function from structural change or chemical reaction. At what level of protein structure or through what chemical reaction does each of the following denaturation factors act?
   a. heat
   b. strong acid
   c. saturated salt solution
   d. organic sovents (e.g. alcohol or chloroform)
   e. heavy metal ions

7. Which are the factors that do not foster α-helix formation? Examples.

8. In 1914, Maillard reported a study of the polymerization of glycine. The amino acid was heated in glycerol solution. The main product of the reaction was found to be 2,5-diketopiperazine. A polypeptide fraction was produced in low yield. The predominant peptides in this fraction were found to be the even peptides, tetraglycine and hexaglycine. Explain.

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9. What type of secondary structure would the following amino acid sequences be *most* likely to have?

   a. polyproline
   b. polyglycine
   c. Ala-Val-Ala-Val-Ala-Val-
   d. His-Gln-Phe-Thr-Trp

10. The tertiary structure of a protein refers to:

   a. Sequence of amino acids
   b. Presence of α-helices or β-sheets
   c. Unique 3 dimensional folding of the molecule
   d. Interaction of a protein with other subunits of enzymes
   e. Interaction of a protein with a nucleic acid

11. What type of interactions does stabilize tertiary structure?

12. A polypeptide has a high pI value. Suggest which amino acids might compose it.

13. The dipeptide gly-asp has three known pK_a values, 2.81, 4.45, and 8.60. Associate each pK_a with the appropriate functional group in the structure of this peptide. Give a practical synthesis of this peptide starting with the amino acids.

14. a. Determine the pI for the following tetrapeptide Lys-Ser-Asp-Ala.
   b. In what direction does the peptide move when placed in an electric field at the following pHs: 4 and 9?

15. Give the structures for the following dipeptides:

   a. Gly-Lys in acidic solution

   b. Val-Asp in basic solution

   c. Ala-Tyr in basic solution

16. Give the structural formula of Phe-Val-Ala-NH_2 at its isoelectric point.

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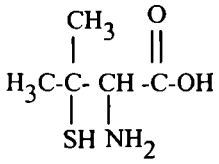
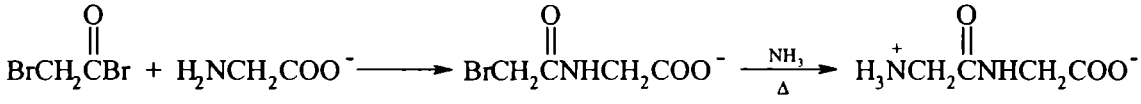
17. Cystinuria is a genetic disorder caused by excessive excretion of cystin into urine. D-penicillamine is effective because penicillamine-cysteine disulfide, which is substantialy more soluble than cystine, is formed. What is the structure of the penicillamine-cysteine disulfide. The structure of penicillamine is:



18. Write out all of the steps in a rational synthesis of the pentapeptide ala-val-phe-ala-ala. For N-protecting groups use the benzyloxycarbonyl group and for coupling use DCC.

19. Propose a synthesis for the pentapeptide in problem 11 using N-carboxy anhydrides. Assume that the necessary anhydrides are commercially available.

20. In 1903, Emil Fischer introduced a rational method for the stepwise contruction of peptides. The process, known as the α-haloacyl method, is outlined below in a synthesis of glycylglycine.



a. Show how the α-haloacyl halide method can be used to synthesize glycyl-L-alanine and glycylglycyl-L-alanine.
b. Which of the α-haloacyl halides would be used to add alanyl or valyl units?
c. If the method is applied to L-alanine using the acyl halides in part (b), what will the product be?
d. What would be the chief problem in applying the α-haloacyl halide method to a fairly complex polypeptide like ala-val-phe-ala-ala

21. A version of solid-phase peptide synthesis (SPPS) uses the *t*-butoxycarbonyl (*t*-Boc) group as α- amino – protecting group. Outline the *t*-Boc protocol for solid phase synthesis of Met-Glu-Ser-Arg tetrapeptide.

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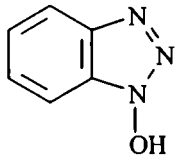
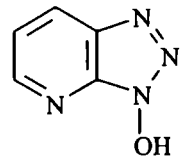
22. Another method of SPPS that has been developed more recently uses the 9-fluorenylmethylcarboxy (Fmoc) group as the amino-protecting group. Outline the Fmoc protocol for solid phase synthesis of Arg-Ser-Ala-Val tetrapeptide.

23. The original coupling reagents used for SPPS were carbodiimides, such as dicyclohexylcarbodiimide (DCCI), N,N'-diisopropylcarbodiimide (DIPCDI). Write the O-acylisoureea intermediares for synthesis of Ala-Ala dipeptide.

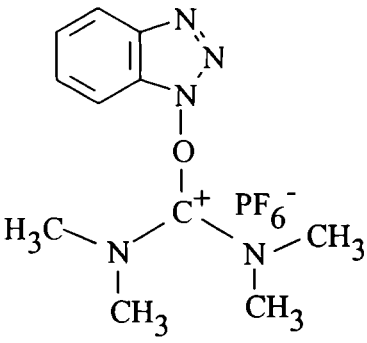
24. The most frequently used coupling reagents are 1-hydroxibenzotriazole (HOBt), 1-hydroxy-7-azabenzotriazole (HOAt) and derivates of them with amidium or phosphonium groups, listed below:



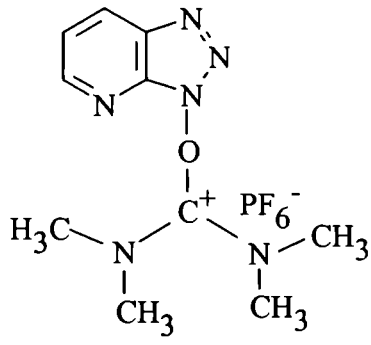
HOBt



HOAt



HBTU



HATU

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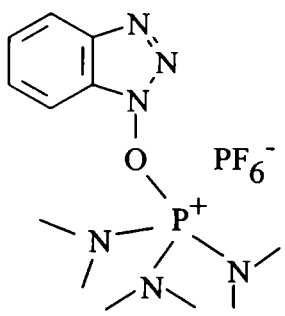
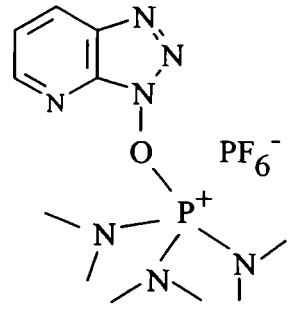


BOP



AOP

Write the structures of the activated esters (use alanine as amino acid).

25. HATU exists in two forms: a guanidinium salt (N-HATU) and an uronium salt (O-HATU). Write the structure of the two isomers.

26. How many dipeptides can be obtained using as starting materials aspartic acid and alanine? Write the structures of each.

27. How many tetrapeptide can be obtained using as starting materials: alanine, leucine, and the dipeptide Phe-Ser? Write the structures of each.

28. a. How many different octapeptides can be made from the 20 naturally occuring amino acids?

    b. How many different proteins containing 100 amino acids can be made from the 20 naturally occuring amino acids?

29. List the amino acids and peptides formed when the following polypeptide is treated with:

    a. trypsin

    b. chymotrypsin

    c. pepsin

    d. thermolysin

    e. cyanogen bromide

    The peptide sequence 13- mers is: trp-met-gly-ile-phe-arg-phe-trp-val-lys-ala-met-ser.

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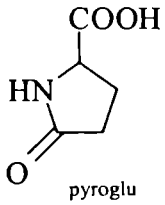
30. The cyanogens bromide method for cleavage of peptide chains involves reaction of the nucleophilic sulfur of a methionine unit with the carbon of BrCN. Write out the complete reaction mechanism.

31. Glutathione is a tripeptide found in most living cells, containing Cys, Glu, and Gly. Treatment with carboxypeptidase liberates Gly. Treatment with DNFB liberates DNP-Cys.
    a. What is the aminoacid sequence in glutathione?
    b. If the glutamic acid forms the peptide link with the side chain carboxyl group, what is the structural formula of glutathione?

32. Pyroglutamic acid, pyroglu, is a cyclic lactam obtained by heating glutamic acid.



pyroglu

This derivative of praline occurs in an important tripeptide, thyrotropin-releasing hormone, TRH, which occurs in brain tissue. It also occurs in the anterior lobe of the pituitary gland where it stimulates the secretion of several other hormones. TRH has been shown to be pyroglutamyl-histidyl-prolineamide. Write out the structure of TRH. A sensitive assay method has been developed that makes use of synthetic hormone. Propose a synthesis of TRH from pyroglutamic acid and other required reagents.

33. A pentapeptide obtained from treatment of a protein with trypsin contains: arginine, glutamic acid, valine, serine and tryptophan. To determine the amino acid sequence, the pentapeptide was treated with Edman reagent three times. The composition of the peptide remaining after each treatment was:
    a. arginine, glutamic acid, valine, serine;
    b. arginine, glutamic acid, serine;
    c. arginine, serine.

    What is the amino acid sequence of the pentapeptide?

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34. Met-enkephalin belong to a group of peptides called opioid peptides (molecules that relieve pain and produce pleasant sensation), found predominantly in nervous tissue cells. The amino acids sequence in Met-enkephalin is Tyr-Gly-Gly-Phe-Met.
    a. What is the net charge and the structure of Met-enkephalin at the following pH: 7, 12?
    b. List the amino acids and peptides when it's treated with chymotripsin ans pepsin.

35. Write the structure of Leu-enkephalin knowing that Leu-enkephalin and Met-enkephalin are pentapeptides that differ only in their C-terminal amino acids residues. List the amino acids and peptides when Leu-enkephalin is treated with thermolysin and pepsin.

36. A polipeptide 5 amino acids long split into various smaller fragments. The identified fragments include His-Gly-Ser, Ala-His, Ala-Ala. Which of the following primary structures can be correct:
    c. Ala-His-Gly-Ser-Ala
    d. Ala-Ala-His-Gly-Ser
    e. His-Gly-Ser-Ala-Ala
    f. Cannot be determined without more information.

37. ACP is a decapeptide, which contain alanine, glutamine, isoleucine, valine, tyrosine, asparagine, aspartic acid, and glycine. Upon enzymatic hydrolysis with chymotrypsin the tripeptide Ile-Asn-Gly and a heptapeptide were obtained. Upon hydrolysis with thermolysin the tetrapeptide Val-Gln-Ala-Ala was obtained along with two other tripeptides. What is the amino acid sequence of the decapeptide ACP?

38. Tyr is not very soluble in water at pH 7 (~0.5g/L).

    a. Would the solubility of the decapeptide $(Tyr)_{10}$ at pH 7 be greater than or less than that of the free amino acid? Explain.

    b. Could a change in pH increase the solubility of Tyr? If so, suggest a pH.

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39. A polypeptide 10 amino acids long split into various smaller fragments. The identified fragments include Ala-Gly- Ser-Glu, Lys-Trp- Arg- Pro, Glu-His-Lys, Asp-Ala-Gly. Which of the following primary structure can be correct:

    c. Ala-Gly-Ser-Glu-Lys-Trp-Arg-Pro-Glu-His
    d. Asp-Ala-Gly-Ser-Glu-His-lys-Trp-Arg-Pro
    e. Ala-Gly-Ser-Glu-His-Lys-Trp-Arg-Pro-Asp
    f. Lys-Trp-Arg-Pro-Glu-His-Lys-Asp-Ala-Gly
    g. None of these

40. Bradykinin is a pain-causing nonapeptide that is released by globulins in blood plasma as a response to toxins in wasp stings. Partial hydrolysis of bradykinin results in the following tripiptides: Ser-Pro-Phe, Gly-Phe-Ser, Pro-Phe-Arg, Arg-Pro-Pro, Pro-Gly-Phe, Pro-Pro-Gly, and Phe-Ser-Pro.

    What is the amino acid sequence in bradykinin?

41. What amino acids or peptides are produced when bradykinin is treated with each of the following reagents:

    a. carboxypeptidase
    b. chymotrypsin
    c. trypsin
    d. DNFB

42. Oxytocin, a pituitary hormone that causes uterine contractions during parturition, is a cyclic nonapeptide joined by a S-S cystine link. Upon acidic hydrolysis seven peptides were obtained: Asn-Cys, Ile-Gln, Cis-Tyr, Leu-Gly, Tyr-Ile-Gln, Gln-Asn-Cys, and Cys-Pro-Leu. Treatment with carboxypeptidase liberates Gly.

    Write the amino acid sequence and the structure of oxytocin.

43. Vasopressin, also known as antidiuretic hormone (ADH), is secreted in response to low blood presure or a high blood Na^+ concentration. Because vasopressin and oxytocin have similar structures, it is not surprising that the functions of the two molecules overlap. Hydrolysis of vasopressin yields Asn-Cys, Phe-Gln, Cis-Tyr, Arg-Gly, Tyr-Phe-Gln, Gln-Asn-Cys, and Cys-Pro-Arg. Treatment with carboxypeptidase liberates Gly.

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Write the amino acid sequence and the structure of vasopressin.

44. A decapeptide undergoes partial hydrolysis to give peptides whose amino acids compositions are shown: Ala, Trp; Val, Pro, Asp; Pro, Val; Ala, Glu; Trp, Ala, Arg; Arg, Gly; Glu, Ala, Leu; Met, Pro, Leu, Glu. Reaction of the intact decapeptide with Edman's reagent releases PTH-Gly. What is the sequence of the decapeptide?

45. Reaction of a polypeptide with carboxypeptidase A releases Met. It undergoes partial hydrolysis to give the following peptides: Ser, Lys, Trp; Gly,His, Ala; Glu, Val, Ser; Leu, Glu, Ser; Met, Ala, Gly; Ser, Lys, Val; Glu, His; Leu, Lys, Trp; Lys, Ser; Glu, His, Val; Trp, Leu, Glu; Ala, Met. What is the sequence of the polypeptide?

46. Gastrins are heptadecapeptides (17 amino acid units) hormones that stimulate the secretion of gastric acid in the stomach of mammals. Feline gastrin has the empirical amino acid composition (ala_2, asp_1,gly_2, glu_5, leu_1, met_1, phe_1, pro_1, trp_2, tyr_1). The peptide was digested with chymotrypsin and four peptide fragments were isolated. The four fragments were sequenced and found to be: glu-gly-pro-trp, gly-trp, met-asp-phe, leu-glu-glu-glu-glu-ala-ala-tyr

    End group analysis revealed that the N-terminal unit is glu and the C-terminal unit is phe. What two structures for feline gastrin are compatible with the foregoing evidence?

47. Hydrolysis of β-endorphin (a peptide containing 31 amino acid residues) produces the following amino acids: Tyr (1), Gly (3), Phe (2), Met, Thr (3), Ser (2), Lys (5), Gln (2), Pro, Leu (2), Val (2), Asn (2), Ala (2), Ile, His and Glu.

    Treatment with carboxypeptidase liberates Gln. Treatment with DNFB liberates DNP-Tyr. Treatment with trypsin produces the following peptides: Lys, Gly-Gln, Asn-Ala-Ile-Val-Lys, Tyr-Gly-Gly-Phe-Met-Thr-Ser-Glu-Lys, Asn-Ala-His-Lys, Ser-Gln-Thr-Pro-Leu-Val-Thr-Leu-Phe-Lys.

    Treatment with chymotrypsin produces the following peptides: Lys-Asn-Ala-Ile-Val-Lys-Asn-Ala-His-Lys-Lys-Gly-Gln, Tyr-Gly-Gly-Phe, Met-Thr-Ser-Glu-Lys-Ser-Gln-Thr-Pro-Leu-Val-Thr-Leu-Phe.

    What is the primary sequence of β-endorphin?

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48. A polypeptide 28 amino acids long has the following sequence: Leu-Leu-Asp-Met-Val-Ala-Leu-Glu-His-Ser-Val-Val-Val-Leu-Gly-Pro-Tyr-Gly-Ala-Met-Val-Thr-His-Leu-Phe-Ala-Glu-Met. It is know that this peptide has two helical segments. Where in the primary sequence would you predict the break between the two α-helices to occur. Why?

49. How long is an α-helix that contains 74 amino acids? Compare this with the length of a fully extended peptide chain containing the same number of amino acids. (The distance between consecutive amino acids in a fully extended chain is 3.5 A)

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STEREOCHEMISTRY

1. a. Enantiomers are stereoisomers which beara mirror-image relationship to each other – L and D alanine.
   b. A stereogenic center is any structural features that gives rise to chirality in a molecule. Asymmetric carbons (carbon atoms with four nonidentical ligands) are a specific example of a stereogenic center.
   c. Racemic modifications are macroscopic assemblies of equal (or very nearly equal) numbers of the two enantiomers.
   d. Stereoisomers that are not enantiomers are diastereoisomers.
   e. The constitution of a compound is the particular combination of bonds between atoms (molecular connectivity) which is characteristic of that structure.
   f. Conformations are discrete molecular arrangements that differ in spatial arrangement as a result of facile rotations about single bonds.

3. Pasteur's most important experimental discovery was the resolution of racemic modification (sodium ammonium salt of (+) tartric acid) into enantiomers. He found several methods to do this, of which the method of mechanical separation is perhaps the most spectacular. In 1861, Pasteur was the first scientist to realize clearly that optical activity was related to molecular dissymmetry. In 1874, two other great chemists, Jacobus Henricus van't Hoff in Holand and Joseph Achille Le Bell in France published articles on the subject.

4. Jean Baptist Biot (like Malus) in 1813 discovers the phenomenon of optical rotation. He shows that the optical rotation is produced not only in the solid (crystalline) state but even in the liquid state (camphor, sugar, tartric acid), as a melt or solution or in vapor phase. He gave the formula for optical rotation (Biot's law).

5. $[\alpha]^{20} = 1.72/ 0.02 \times 1 = 86 g^{-1} mL^{-1} dm^{-1}$

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6. If the fraction of (+) enantiomer is x the fraction of (-) enantiomer will be (1-x).

The apparent specific rotation is described by the following equation:

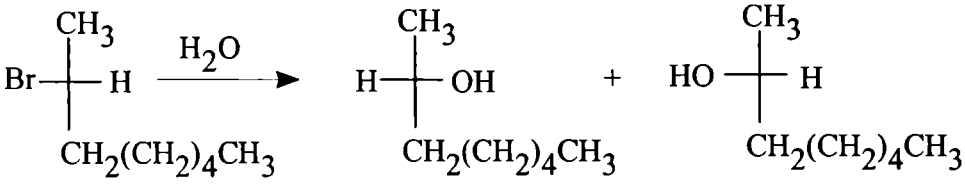
$$x\,(+[\alpha]) + (1-x)(-[\alpha]) = [\alpha]_{apparent}$$

a. $0.25(158) + 0.75(-158) = -79^{o}$

b. $0.5(158) + 0.5(-158) = 0$

c. $0.75(158) + 0.25(-158) = 79^{o}$

7.



S (+)-2-octanol R(-)-2-octanol

If x is the fraction of (+) enantiomer then:

$x(89) + (1-x)(-89) = +59$

$178x = 148;\ x = 0.83$

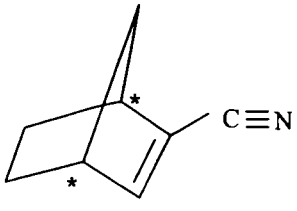
83% of the reaction is proceeding through a mechanism involving stereochemical inversion.

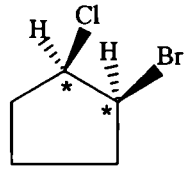
9. a. Yes, those having a single chiral center, alanine

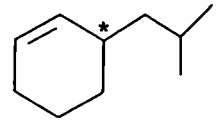
b. Yes, in particular achiral cis-trans isomers, cis and trans 2,3-dichlorobutene

c. Yes, in general any compound with two or more chiral center will be in this class, ribose

10. a, b, c – none asymetric carbone; the molecules have planes of symetry.

d. 

e. 

f. 

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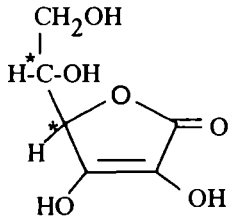
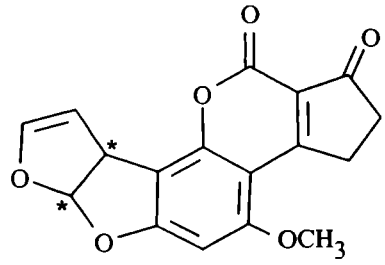
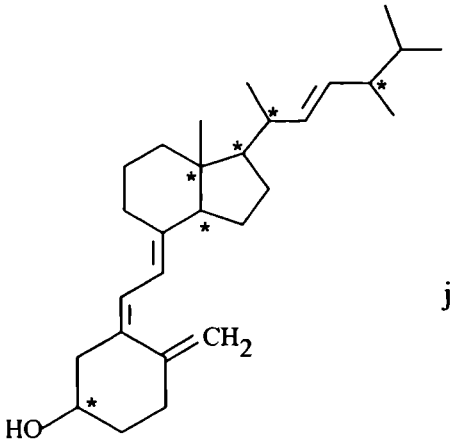
g. 

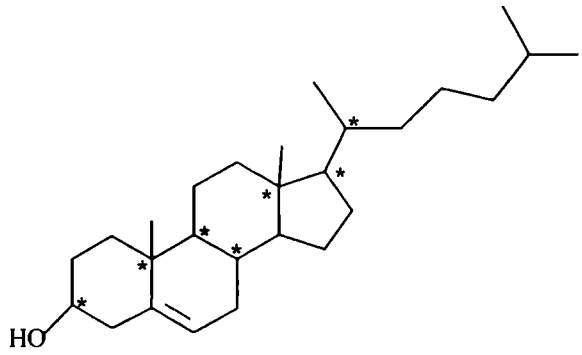
Ascorbic acid

h. 

Aflatoxin

i. 

Vitamine D_2

j. 

Cholesterol

11. a. $-OC_2H_5$, -OCH_3, -OH, -COOH,
    b. -OH, –F, -COOH, -H
    c. -OH, - C^* abc (R), –C^* abc (S), -H

12. a, b, d, e – are optical inactive (the molecules have planes of symmetry)
    c, f – exhibit optical activity

13. One simple test for chirality of substituted cycloalkanes is to represent the ring in plane form. If the planar form is achiral because of a summetry element, the compound will not exist as an enantiomerically biased sample, even if individual conformers may be chiral.
    Achiral structures: a, c, e, f, g, j, k, l, n, o
    Chiral structures: b, d, h, m

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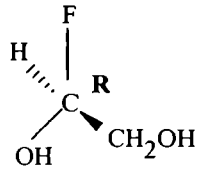
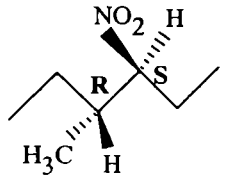
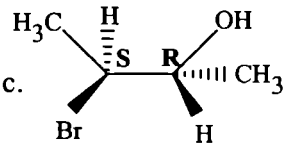
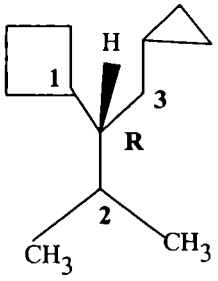
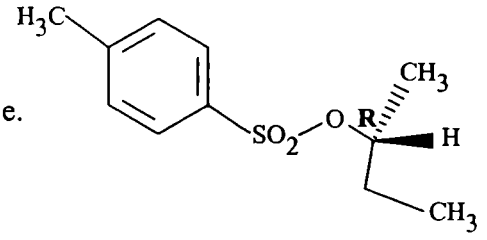
14.

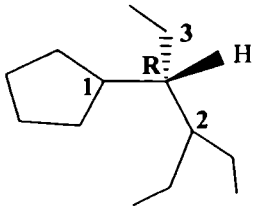
a. 

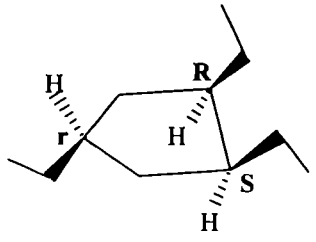
b. 

c. 

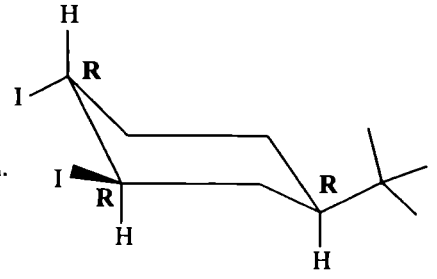
d. 

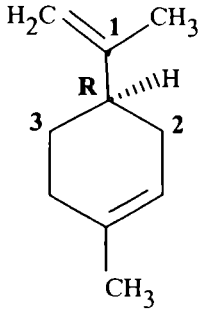
e. 

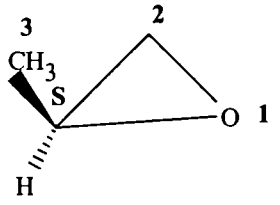
f. 

g. 

o.i

h. 

i. 

j. 

15. a. (2R, 3S) isocitric acid

b. (2S, 3R) isocitric acid

c. (2R, 3R) alloisocitric acid

d. (2S, 3R) alloisocitric acid

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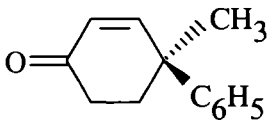
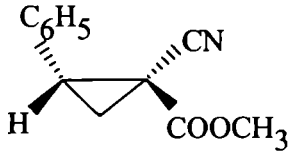
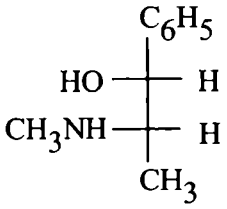
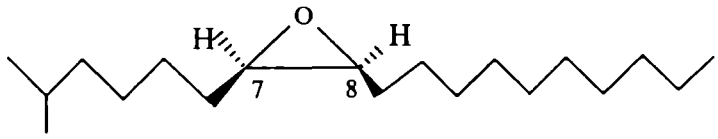
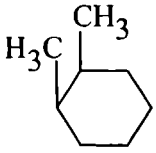
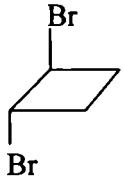
16. a. 

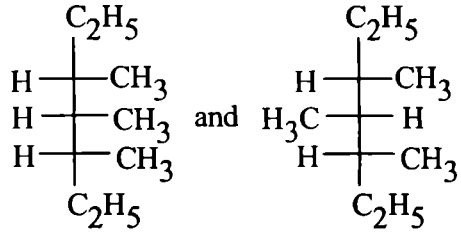
b. 

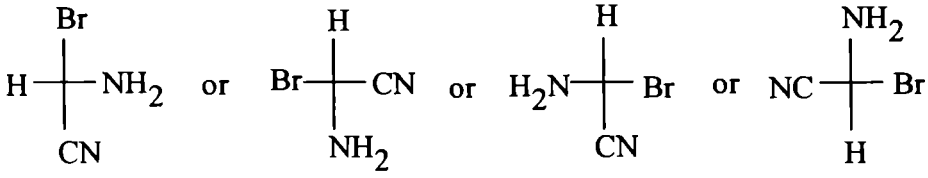
c. 

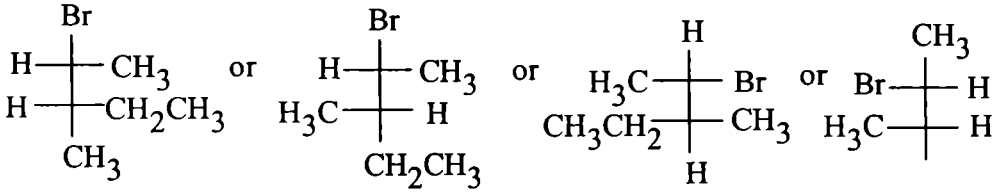
d. 

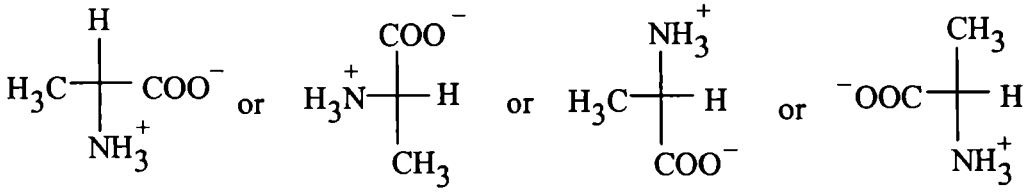
e. 

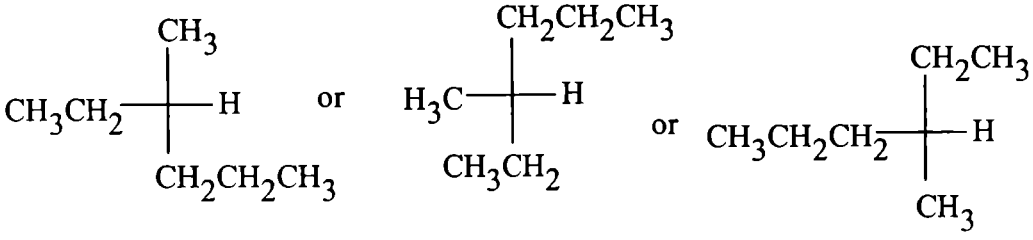
f. 

g. 

17. a. 

b. 

c. 

d. 

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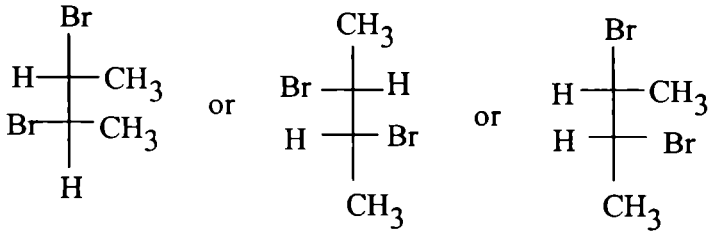
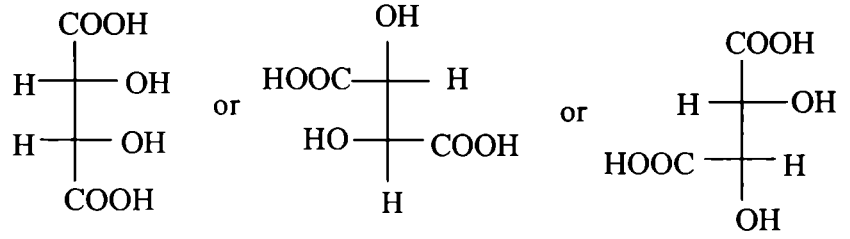
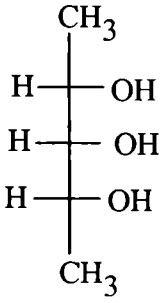
e. 

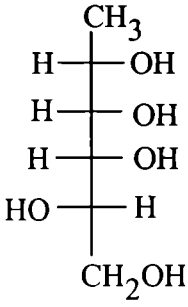
f. 

18. None of them. The correct Fisher projection is:



19. a. enantiomers
    b. identical compounds
    c. diastereoisomers
    d. epimers

20. c. Epimers at C_3. The Fisher projection is:



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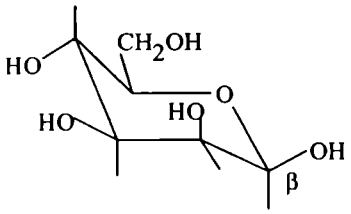
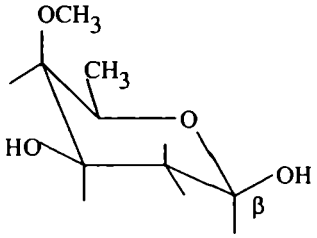
21. a.



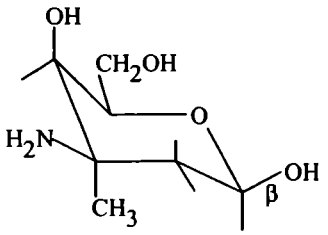
β– D-mannopyranose

b.



β– D-chromopyranose A

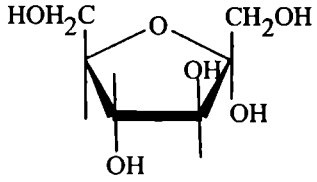
c.



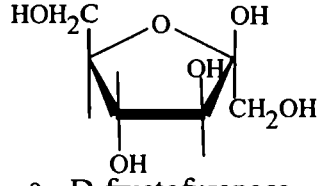
β– D-amine-vancopyranose

22.

a.

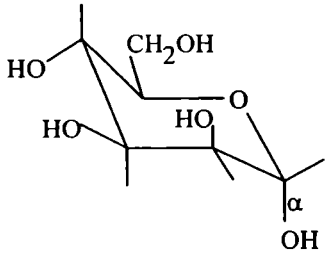


α–D-fructofuranose
less stable

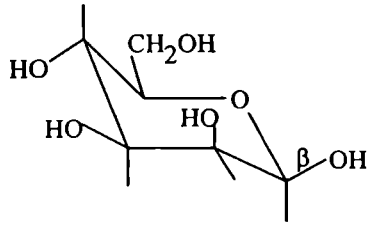


β– D-fructofuranose
more stable

b.

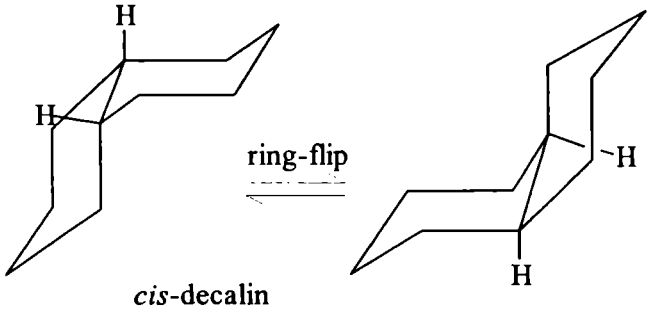


α–D-mannopyranose
less stable

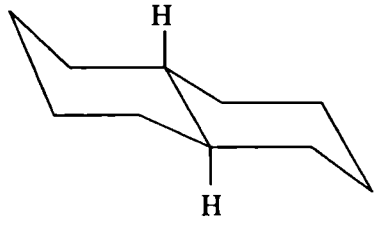


β– D-mannopyranose
more stable

c.



cis-decalin
less stable



trans-decalin
more stable

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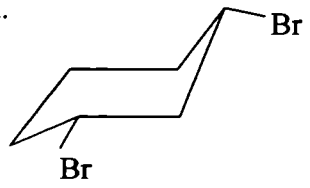
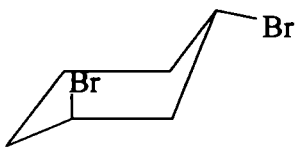
d.



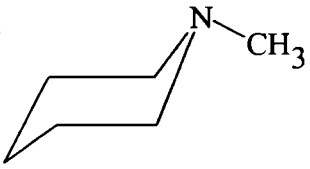
cis-1,3-dibromocyclohexane
more stable



trans-1,3-dibromocyclohexane
less stable

23.

a.



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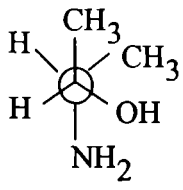
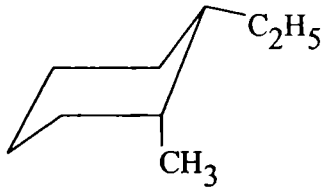
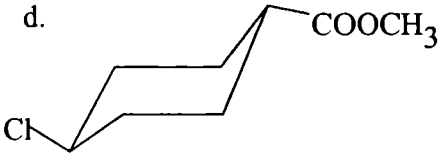


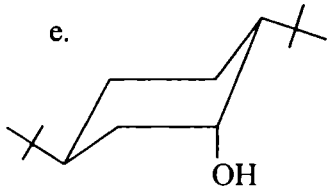
c.



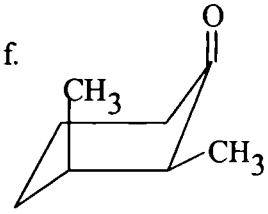
d.



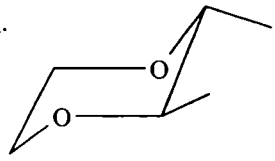
e.



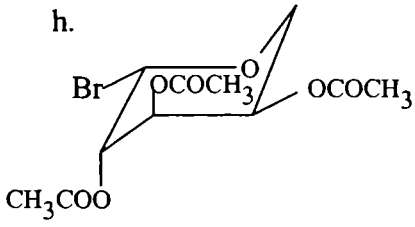
f.



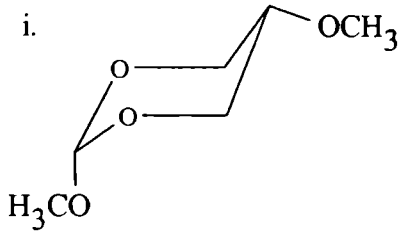
g.



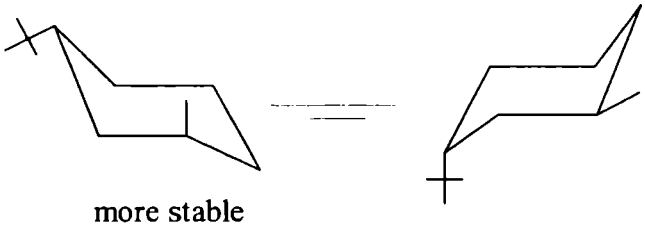
h.



i.



24. The conformations in which the *tert*-buthyl group is equatorial would be more stable.



more stable

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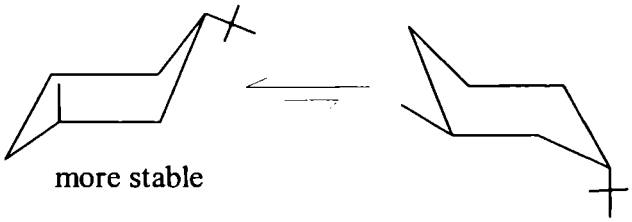

25. Chiral objects: b, c, d, f.

27. The property of chirality is determined by overall molecular topology, and there are many molecules that are chiral even though they do not possess an asymmetrycally substituted atom.

    a. R- (-)-glutinic acid
    b. R– (-)-1,3-dimethylalllene
    c. S- (+)-1,1'-binaphtyl
    d. R- (+)-2,2'-diamino-6, 6'-dimethylbiphenyl
    e. R- (-)-E-cyclooctene
    f. S- (+)-spiro [3,3]-hepta-1,5-diene

    There is no direct relationship between the configurational descriptors R and S or D and L and the sign of rotation of the molecule. R or S molecules can have either + or – signs for rotation, as can D or L molecules.

28. optical active: a, d
    optical inactive: b, c

29. When a stereogenic center is tricoordinate, as is the case of sulfoxides, sulphonium salts, and phosphines, then a "phantom atom" of atomic number zero is taken to occupy the lowest-priority site of a presumed tetrahedral atom.

    a. R-enantiomer
    b. R-enantiomer
    c. S-enantiomer
    d. S-enantiomer
    e. R-enantiomer

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30. a. diastereoisomers

b. enantiomers

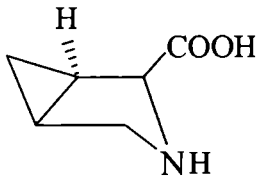
c. diastereoisomers (cis-trans)

d. enantiomers

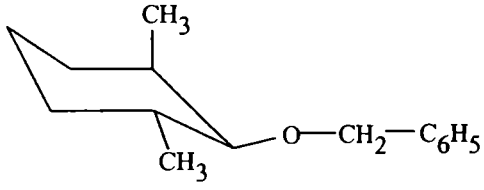
e. enantiomers

f. identical compounds

31.



32.

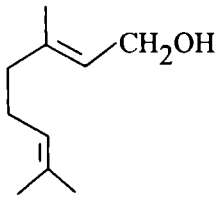


33. a. (z)-3-decenoic acid (the sex feromone of the furniture carpet beetle)

b. Methyl (2E, 6E, 10Z)-10,11-epoxy-3, 7,11-trimethyltridecadienoate (the juvenile hormone of the tobacco hornworm)

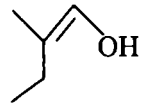
c. (2Z, 4Z, 6E, 8E)-9-(3'-furyl)-2,6-dimethylnona-2,4,6,8-tetraen-4-olide (dihydrofreelingyne)

34. a.



b.

c.



d.

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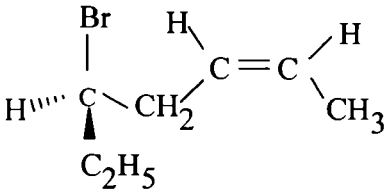
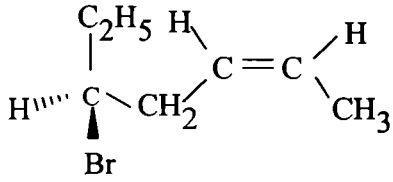
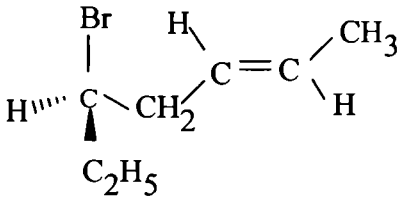
35. The compound has 4 stereoisomers:



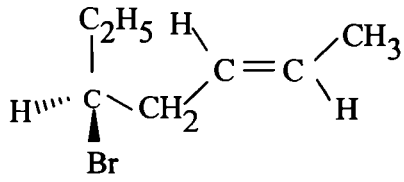
(Z)-5-(R)-bromo-2-heptene



(Z)-5-(S)-bromo-2-heptene



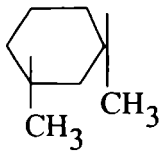
(E)-5-(R)-bromo-2-heptene

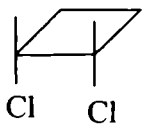


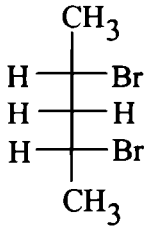
(E)-5-(S)-bromo-2-heptene

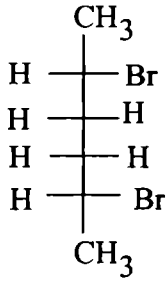
36. a. It doesn't has any chirality centers.

b. Each of the chirality centers are not bonded to the same four substituents.

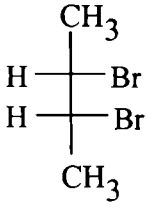
c. 

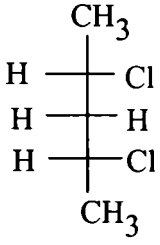
d. 

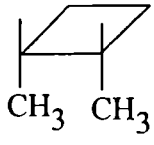
e. 

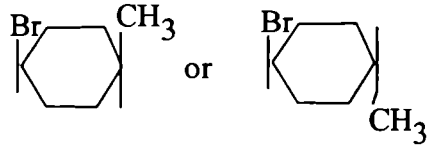
f. 

37. a, c, d, e are the compounds which have a stereoisomer that is achiral. The structures of these stereoisomers are the following:









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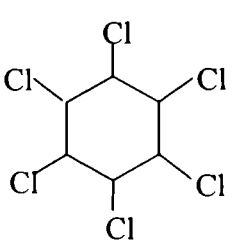
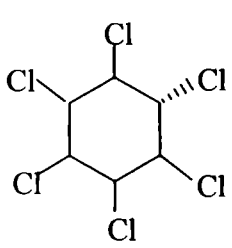
38. a.


1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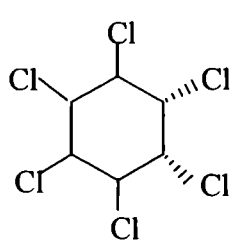
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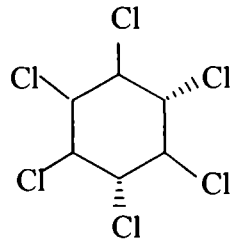
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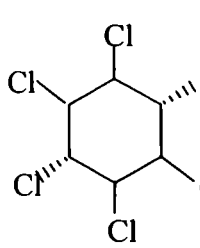
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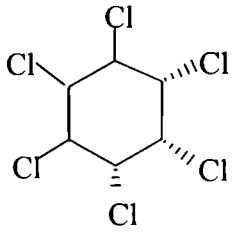
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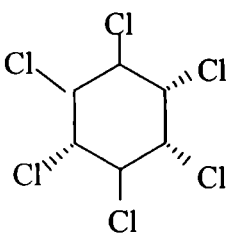
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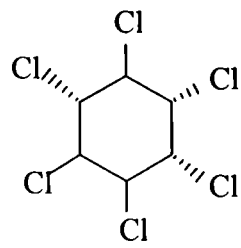
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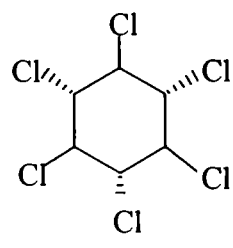
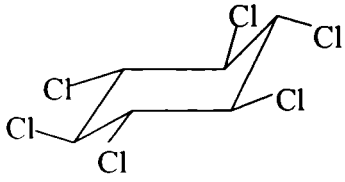
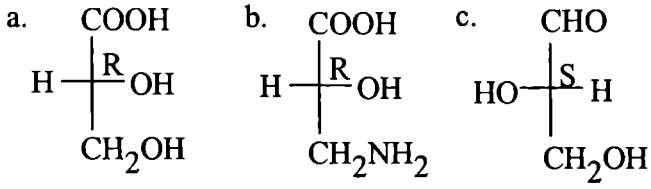

9

b. **7** and **8** are enantiomers; the others are achiral compounds (the molecules have simmetry planes)

c. The most stable conformation is for the compound **9**, when all substituents are equatorial:



39.



40. (+)-2-Methylbutanoic acid has the configuration shown below because it was formed from (S)-(-)-2-methyl-1-butanol without breaking any bonds to the chirality center.

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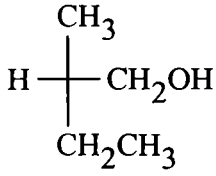
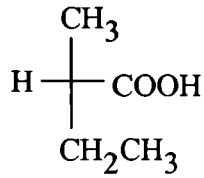


(S)-(-)-2-methyl-1-butanol



(+)-2-methylbutanoic acid

It has the S configuration.Therefore, (-)-2-methylbutanoic acid has R configuration.

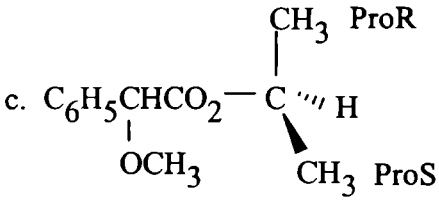
41. The product will have the S configuration. The reaction does not affect the stereogenic center.

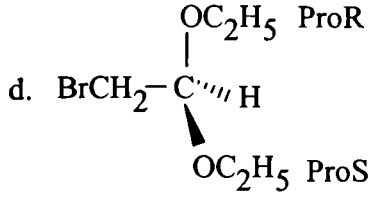
42. diatereotopic hydrogens: a, e, f

homotopic hydrogens: b, d

enantiotopic hydrogen: c

43. a, b – none diastereotopic atoms or groups





44. a. Yes, *cis-trans* isomers

b. Not normally. However, separation of the two conformations has been effected at –150°C

c. Yes, *cis-trans* isomers

d. No, because of rapid nitrogen inversion. However, *cis-trans* isomerism can be seen in the NMR spectrum (the isomers interconvert rapidily) and, in the case of the similar N-chloro compound, isomers have actually been separated.

e. Yes

f. Not resolved (tertiary amines)

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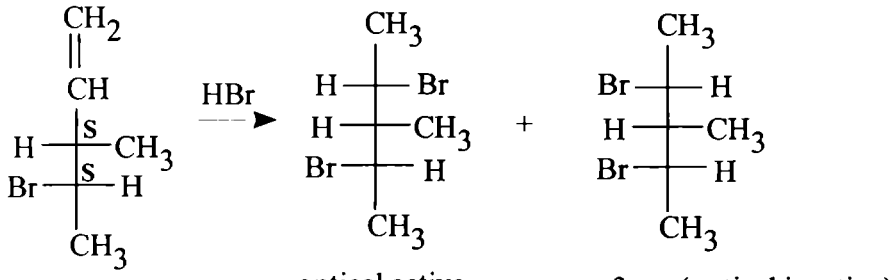
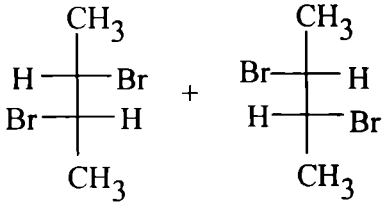
46.



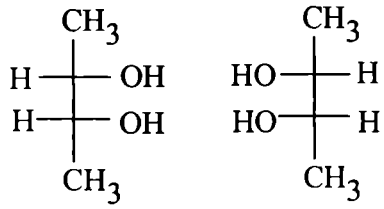
47. One wat to determine what stereoisomers are obtained from a reaction that creates a product with two chirality centers is the mnemonic **"cis-syn-erithro",** which is easy to remember because all three terms means "on the same side". You can change any two of the terms, but you cannot change just one. (For example, **trans-anti-erithro, trans-syn-threo,** and **cis- anti-threo** are allowed, But trans-syn-erithro is not allowed)

a.



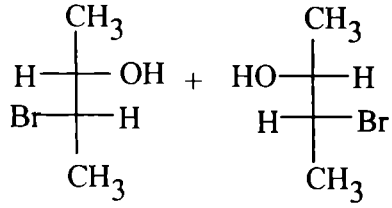
enantiomers

b.



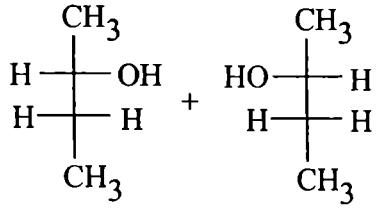
identical compounds (meso)

c.



enantiomers

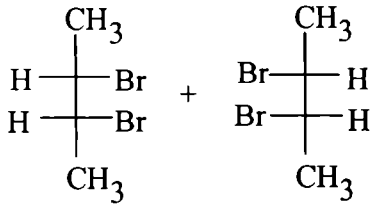
d.



enantiomers

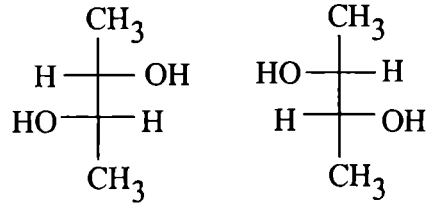
48.

a.



identical compounds (meso)

b.



enantiomers

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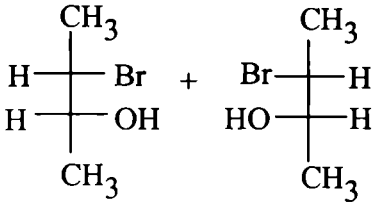
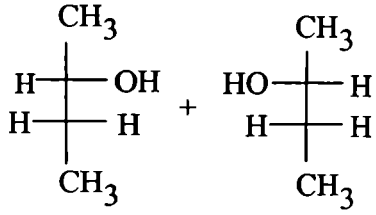
c.



enantiomers

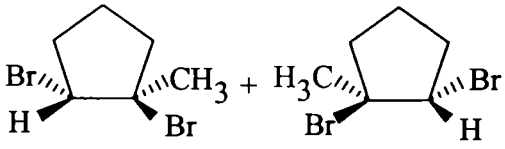
d.



enantiomers

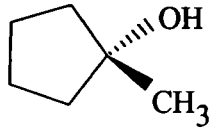
49.

a.



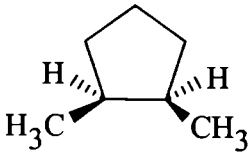
enantiomers

b.



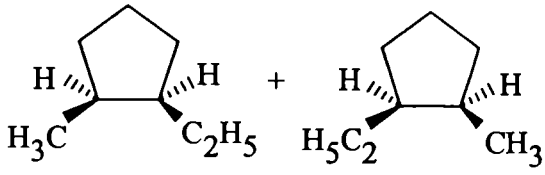
achiral (plane of simmetry)

c.



achiral (plane of simmetry)

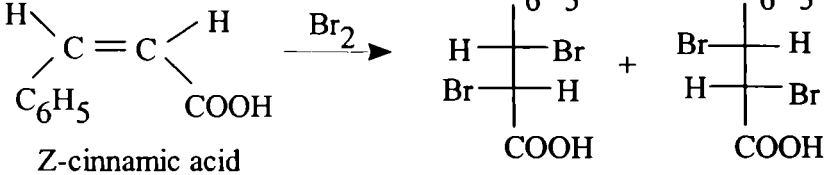
d.



enantiomers

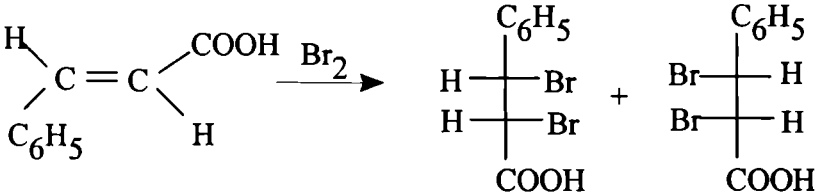
50.

a.



Z-cinnamic acid

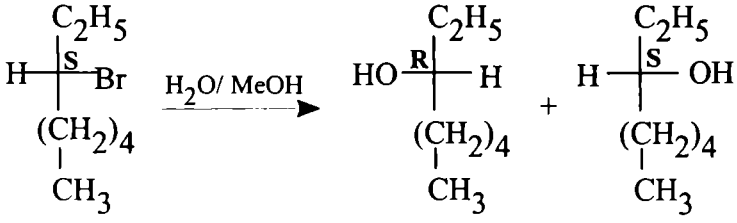
threo (enantiomers)



E-cinnamic acid

erithro (enantiomers)

b.



major product

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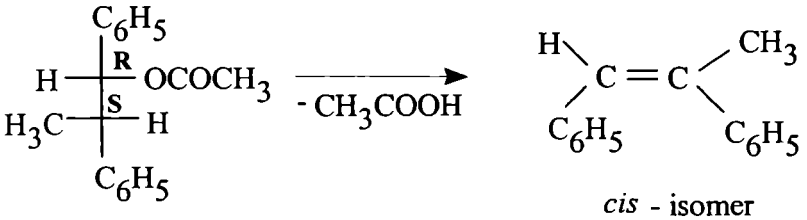
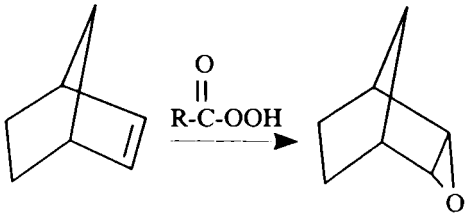
c.



cis - isomer

d.



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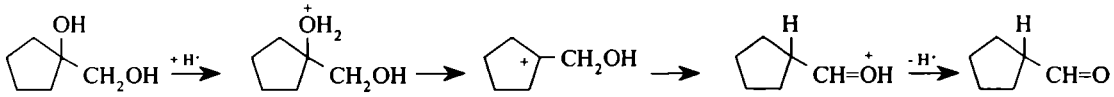
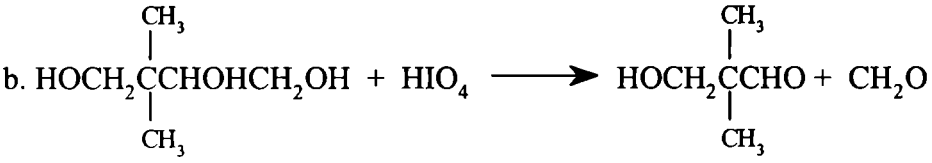
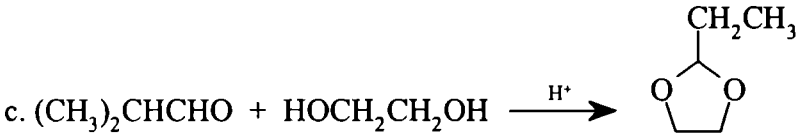
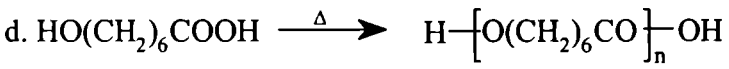
3.

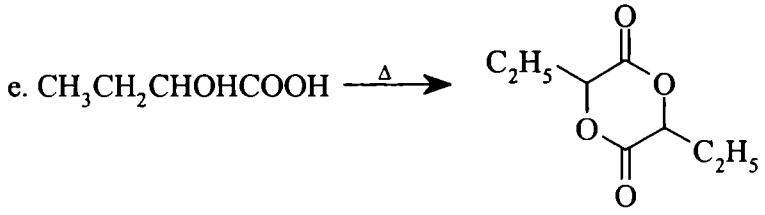
a. 

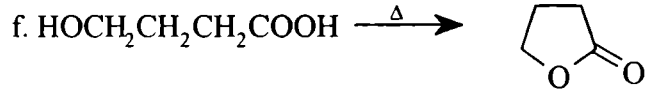
(The oxonium ion is more stable than the tertiary carbocation)

b. 

c. 

d. 

e. 

f. 

4. a. *meso*-cyclodecanediol

b. (±)-cyclodecanediol

c. (±)-epoxy-cyclodecane

d. (±)-cyclodecanediol

e. *meso*-cyclodecanediol

f. *meso*-epoxy-cyclodecane

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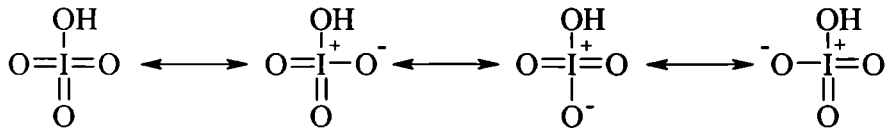
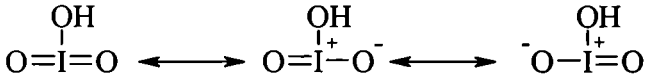
5. a.

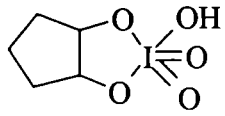


periodic acid



iodic acid

b. The intermediate:

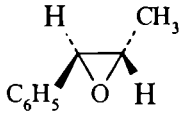


is formed much more easily with *cis*-1,2-cyclopentanediol.

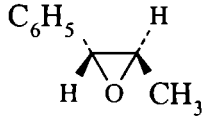
c. By oxidation with HIO_4, 1,2,3-pentanetriol yields two compounds (CH_2O, HCOOH, and CH_3CH_2CHO) , whereas 1,2,4-pentanetriol, just two (CH_2O and $CH_3CHOHCH_2CHO$).

6. a. cyclohexene: b. 1-butene; c. *cis*-2-pentene; d. *trans*-2-pentene.

7. a. racemic mixture

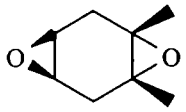


R,R

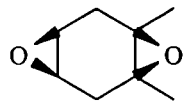


S,S

b.



anti-1:2,4:5-diepoxy-
1,2-dimethylcyclohexane



syn-1:2,4:5-diepoxy-
1,2-dimethylcyclohexane

8. a. (±)-2-methyl, 2,3-pentanediol;

b. (±)-1-hydroxymethylcyclohexanol.

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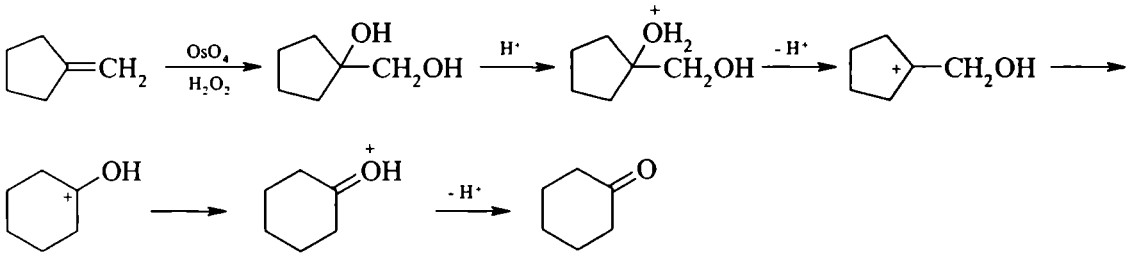
9. a. (±)-2,3-butanediol;

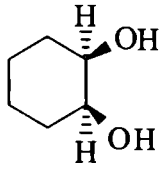
   b. *meso*-2,3-butanediol;

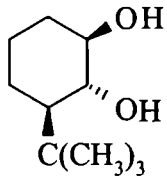
   c. (±)-erythro-2,3-pentanediol; (±)-threo-2,3-pentanediol.

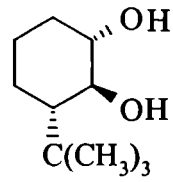
10. Methylenecyclopentane:



11.

a. 

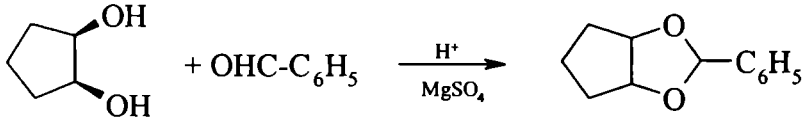
b. 

c. 

12. In the first row of reactions, an oxonium ion is formed, which is more stable than the carbocation that would be formed in the second row of reactions.

13. Dehydration under acidic conditions occurs only in the case of *cis* cyclic diols.

14.



The acetalization reaction is reversible; the anhydrous $MgSO_4$ is hygroscopic and removes the water from the reaction mixture, shifting the equilibrium towards the formation of the acetal. The *trans* isomer cannot form an acetal due to the ring strain that would result in the acetalic ring.

15. In liquid NH_3, Li donated electrons, while NH_3 donates protons; lithium amidide is formed:

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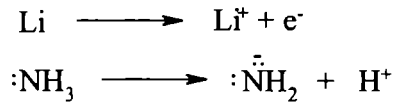
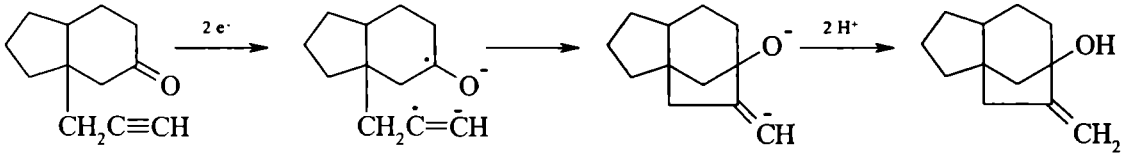


The free electrons attack the substance:



16.

a. acetone → pinacol → pinacolone →oxidation

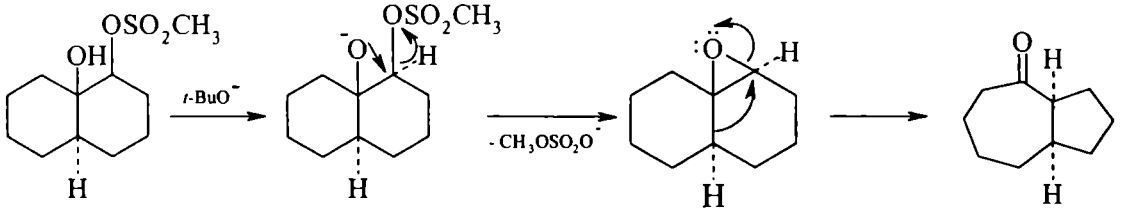
b. propanoic acid → 2-bromo-propanoic acid + propanal + Zn (Reformatsky reaction of β-hydroxy acids synthesis)

c. benzoin condensation, followed by reduction

d. addition of HCN, hydrolysis → α-hydroxy acid → lactide

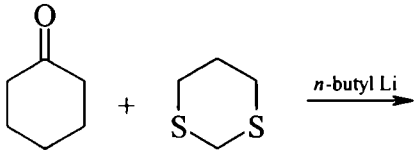
e. propionic acid → ester → acyloin

17.



18. Start from:

a.



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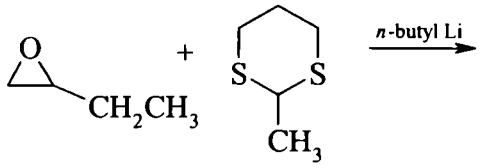
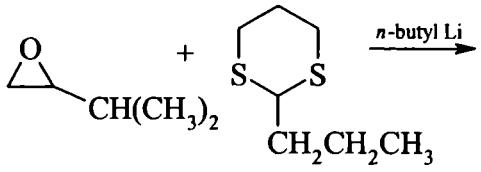
b.



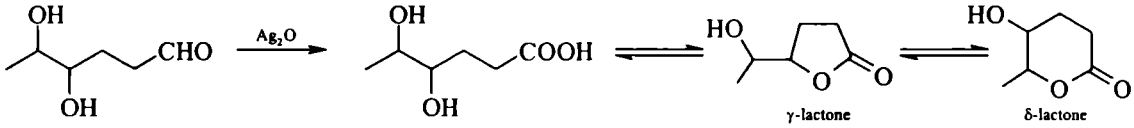
c.



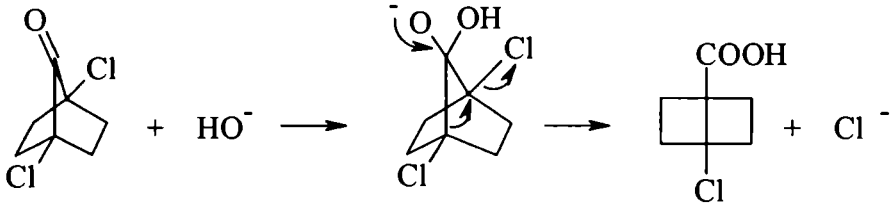
19. Because an extended conjugated system results.

20. a. The six-membered ring predominates.

b. The γ-lactone predominates.



21.



1,4-dichloro-[2,2,1]-bicycloheptan-7-one

4-chloro-[2,2,0]-bicyclohexane carboxylic acid

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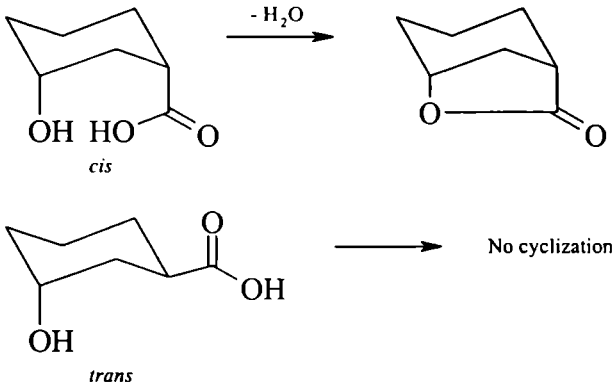
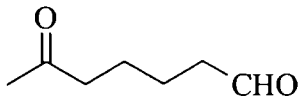
22.



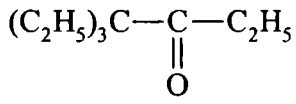
The two functional groups are proximal in the *cis* isomer, and the lactonization is favored. In the *trans* isomer the two functional groups are too distant to interact.

23.

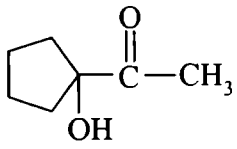
a.



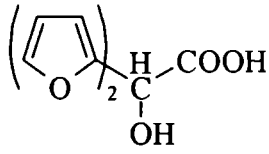
b.



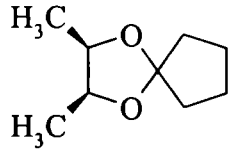
c.



d.

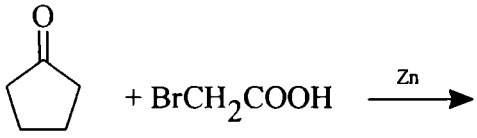


e.



24.

a.



(Reformatsky reaction of obtaining β-hydroxy acids).

b. $(CH_3)_2CHCOOC_2H_5 \xrightarrow{\text{acyloin condensation}} (CH_3)_2CHCOCHOHCH(CH_3)_2 \xrightarrow{Cu(OAc)_2} (CH_3)_2CHCOCOCH(CH_3)_2$

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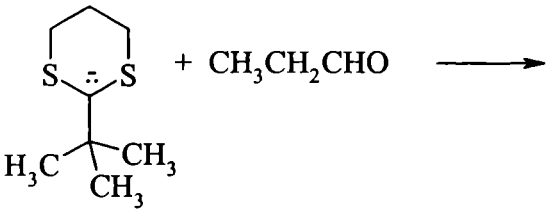
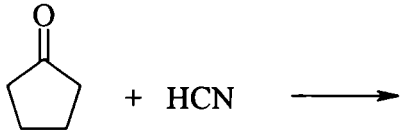
c.

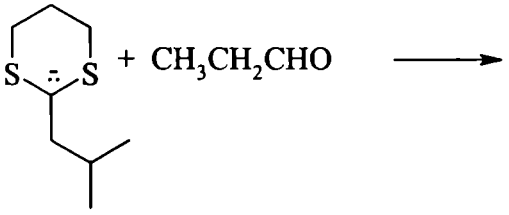


d. 3-pentanone → pinacol reaction → pinacol rearrangement

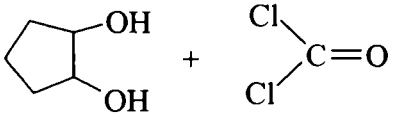
e.



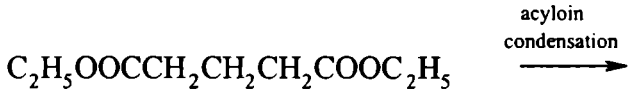
f.



g.



h.



i. cyclopentanone → pinacol reaction → pinacol rearrangement → reduction

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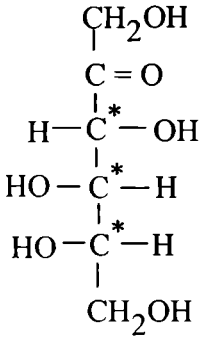
CARBOHYDRATES

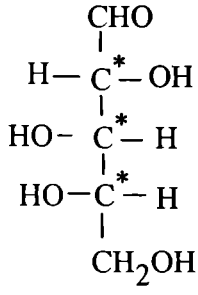
1. a. Epimers are monosaccharides that differ in configuration at only one carbon.
   b. Anomers are two cyclic sugars that differ in configuration only at tha carbon that is in the carbonyl carbon in the open-chain form.
   c. Diastereoisomer is a configurational stereoisomer that is not an enantiomer.
   d. A monosaccharide (simple carbohydrate) is a single sugar molecule.
   e. A reducing sugar is a sugar that can be oxidized by reagents such as Ag^+ or Br_2. Reducing sugars are in equilibrium with the open-chain aldoseor ketose.

2. In D family sugars the OH on the chiral carbon farthest from the carbonyl is on the right in a Fisher projection. There is no direct relationship between the configurational descriptors D and L and the sign of rotation of the molecule. So both (+) glucose and (-) fructose are D sugars despite their rotation of plan-polarized light in opposite directions.

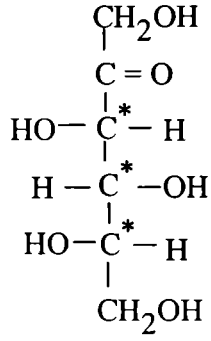
3. a.



L - Fructose



L - Arabinose



L - Sorbose

   b. $2^3 = 8$ stereoisomers

4. a. epimers
   b. enantiomers
   c. diastereoisomers
   d. an aldose-ketose pair

5. a. 2R, 3S, 4R, 5R-6 pentahydroxihexanal
   b. 3S, 4R, 5R-1,6-pentahydroxihexane-2-ona

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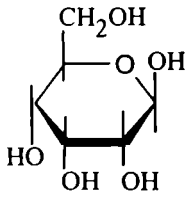
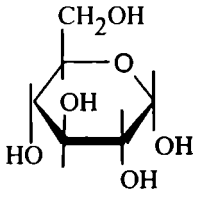
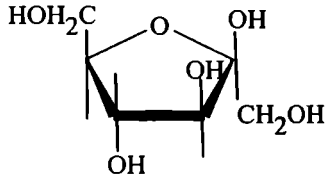
c. 2R, 3R, 4R –5-tetrahydroxipentanal

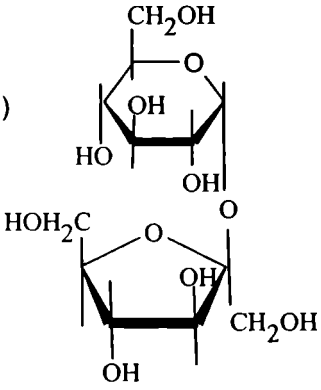
d. 3S, 4R-5-trihydroxipentanal

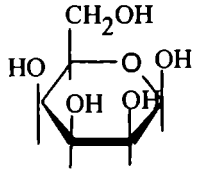
6.

a) 

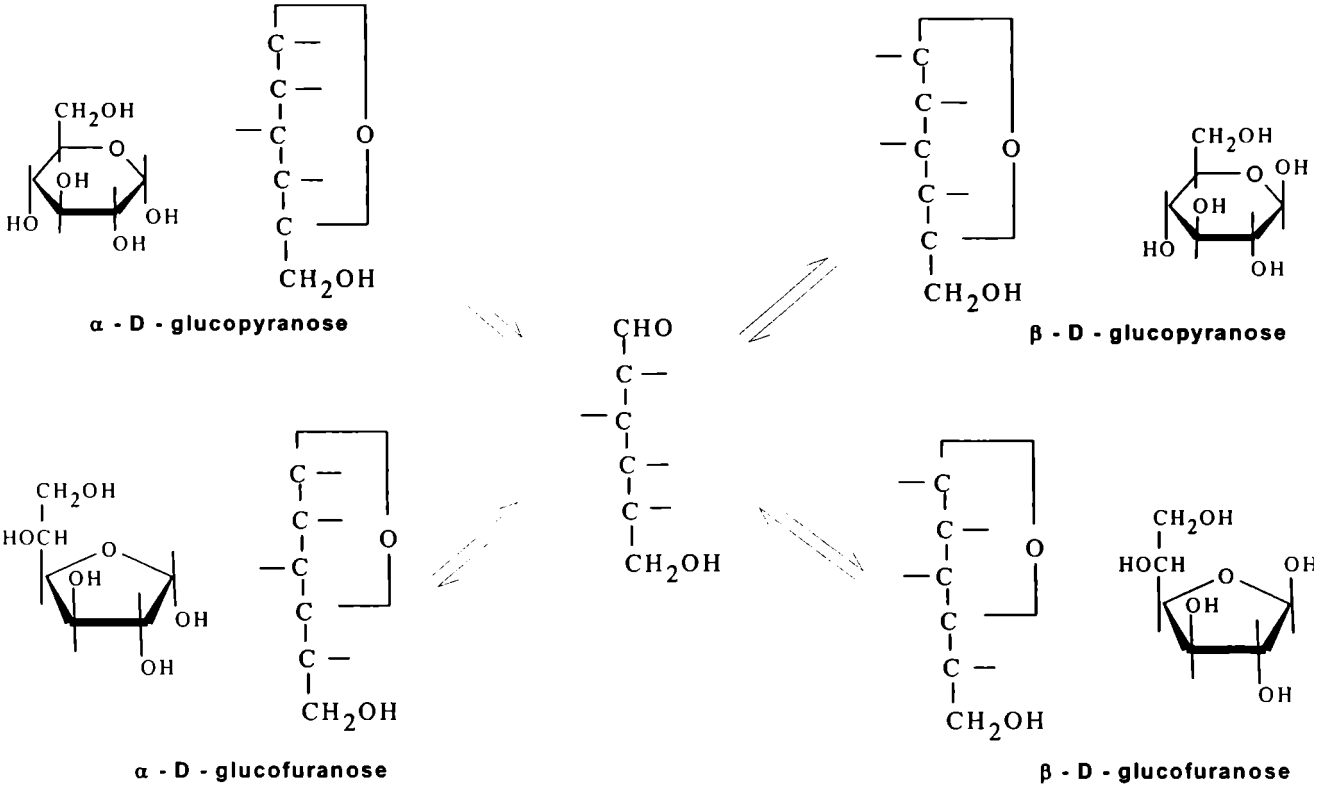
b) 

c) 

d) 

e) 

7. a.



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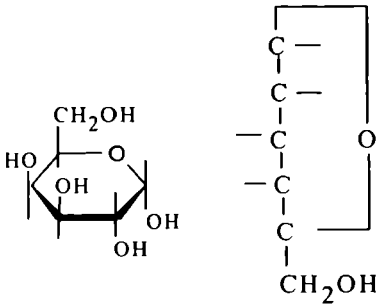
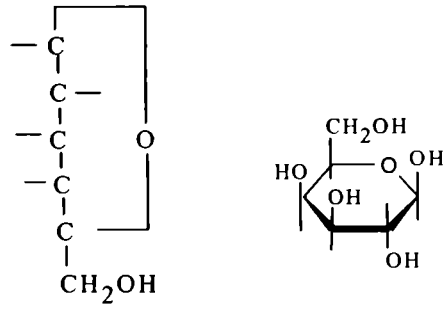
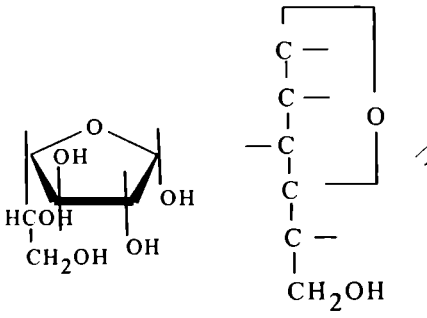
b.



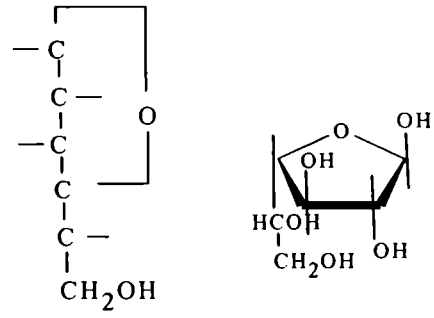
α - D - galactopyranose



β - D - galactopyranose

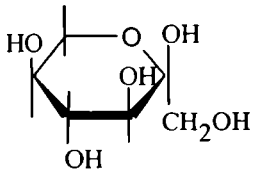


α - D - galactofuranose

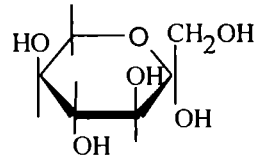


β - D - galactofuranose

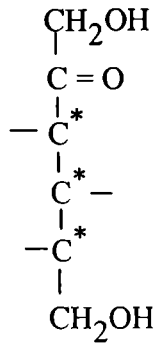
c.



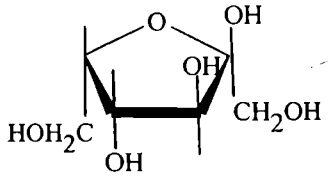
α - L - sorbopyranose



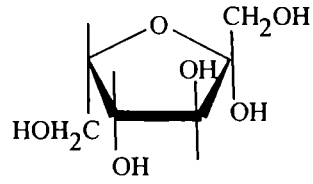
β - L - sorbopyranose



L - Sorbose



α - L - sorbofuranose



β - L - sorbofuranose

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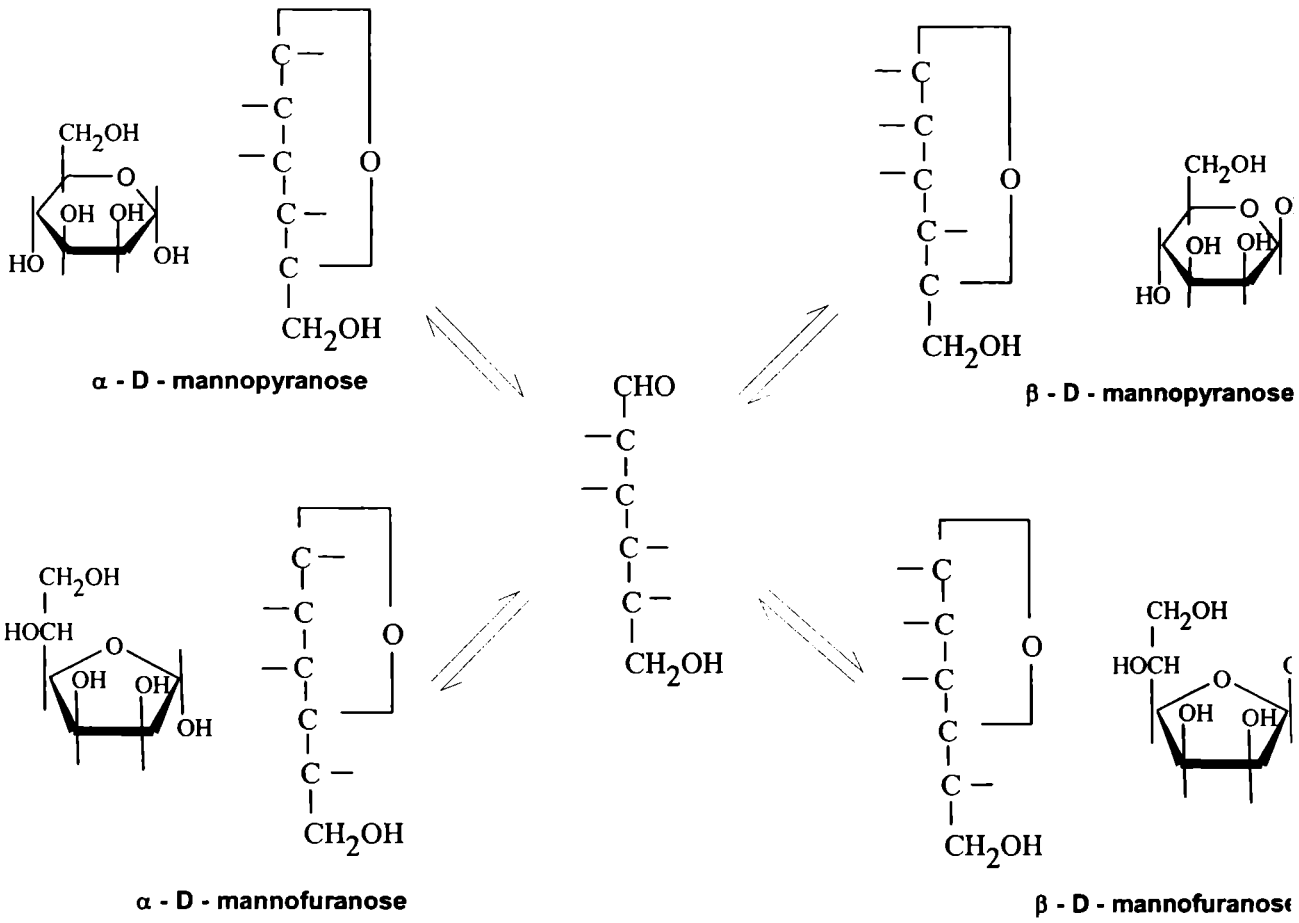
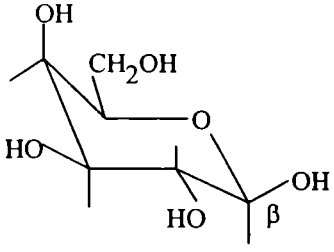
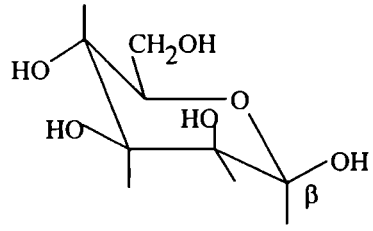
d.



8.



β– D-galactopyranose
more stable (annomeric effect)



β– D-mannopyranose

9. When $-CH_2OH$ group of D-idopyranose is equatorial, all other –OH groups are axial. The conformers are more stable when the -OH groups are equatorial. So, D-idopyranose exist primarily in a conformation with an axial $-CH_2OH$ group.

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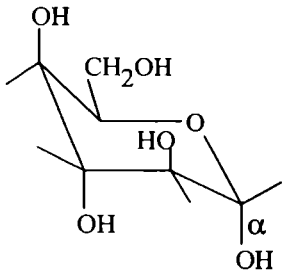
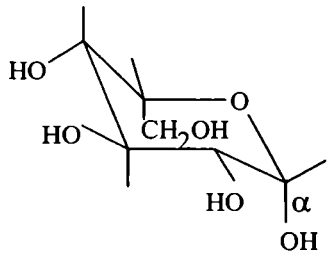


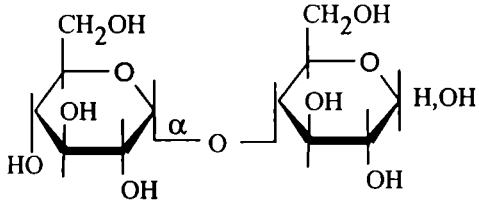
α–D-idopyranose



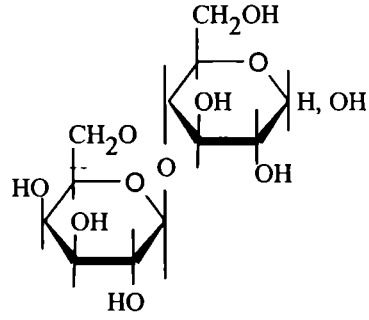
α–D-idopyranose

10. a. All sugars with free anomeric hydroxyl group undergo mutarotation.

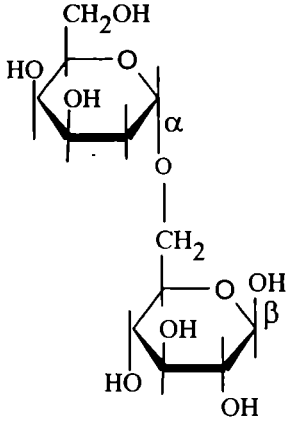
b. The structures of the sugars are presented below:



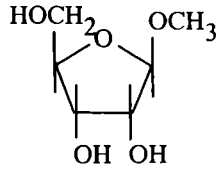
4-(α-D-glucopyranosyl)-D-glucopyranose



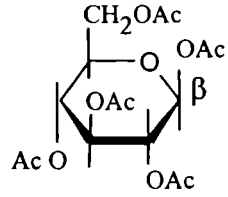
4-(β-D-galactopyranosyl)-D-glucopyranose



6-(α -D-galactopyranosyl)-β–D-glucopyranose



β –O–Methyl-D-ribofuranose



β –pentaacetyl-D-glucofuranose

c. Are reducing sugars all sugars that undergo mutarotation.

d. Reaction with Benedict, Fehling, Tollens reagents.

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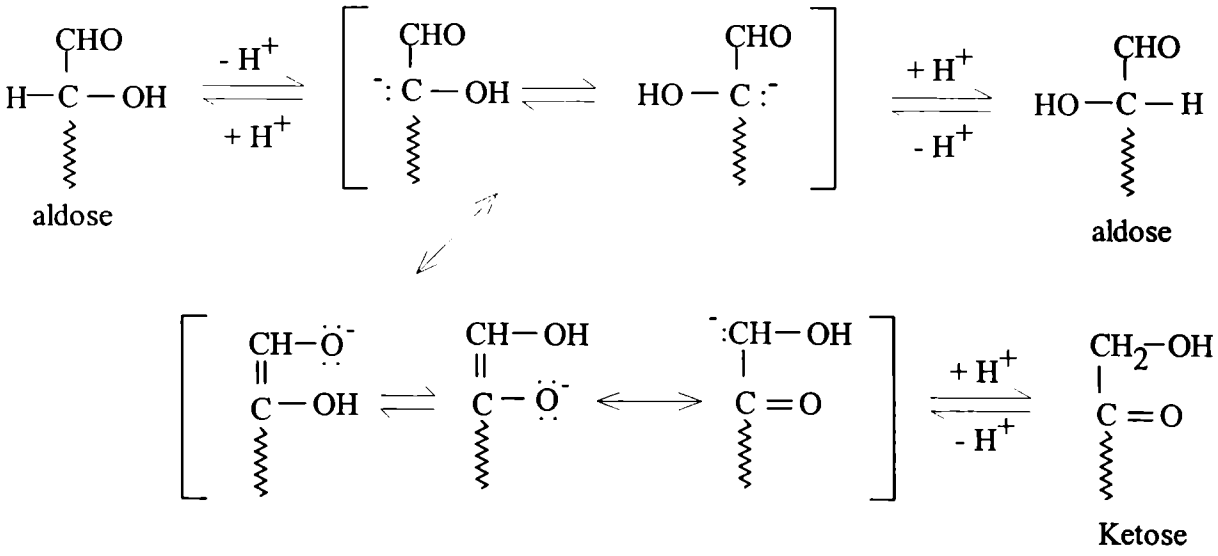
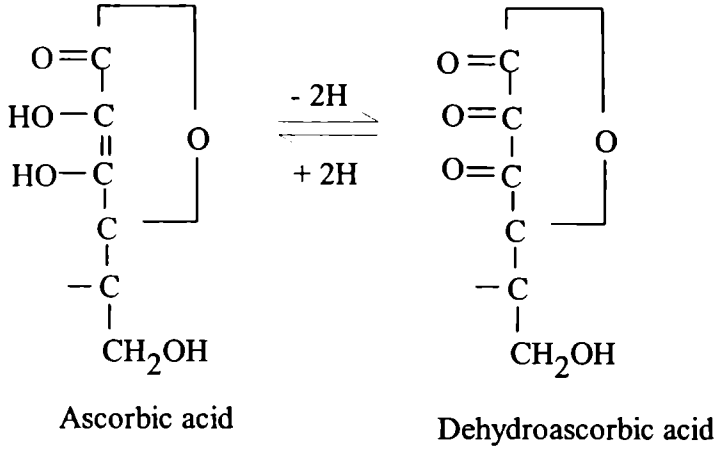
12. Bruyn-van-Eckenstein transposition:



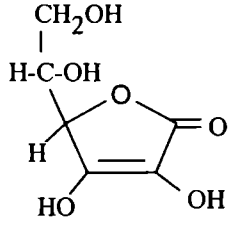
14. c.



Ascorbic acid

Dehydroascorbic acid

15.



4.2 11.6

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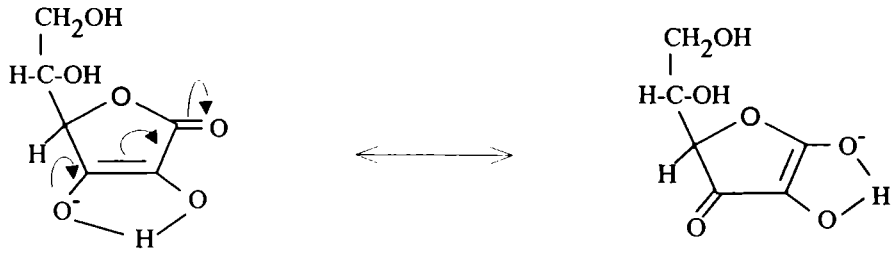
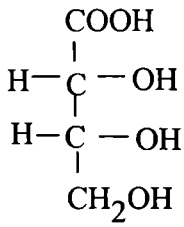


The conjugated base is stabilized by conjugation (6e$^-$ involved).

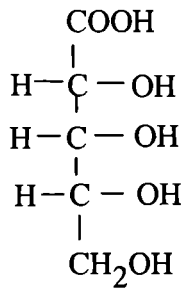
The hydrogen atom of the second hydroxyl group (pK=11.6) is involved in a hydrogen bond (see above), which diminuished drastic its acidity.

16.

a. 

erithronic acid

b. none

c. 

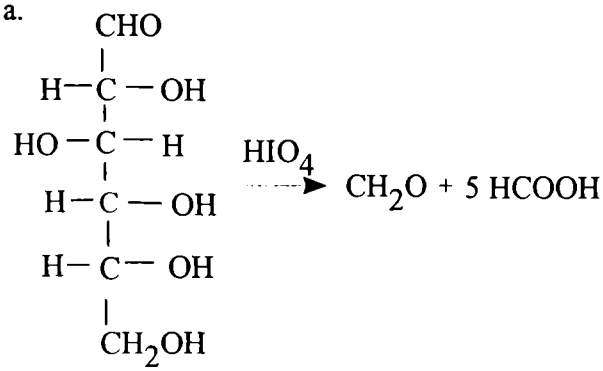
ribonic acid

d. none

17. Allose and galactose (both D and L configuration) give meso-aldaric acids upon oxidation with hot nitric acid.

18. D-allose and L-allose, D-altrose and D-talose, L-altrose and L-talose L-galactose and D-galactose are the pairs of aldohexoses that are oxidized to identical aldaric acids.

19.

a. 

D-glucose

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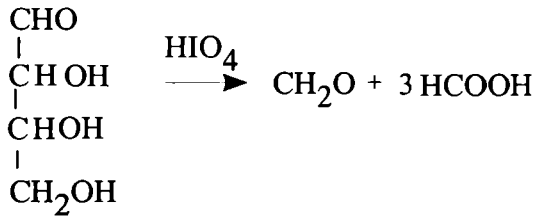
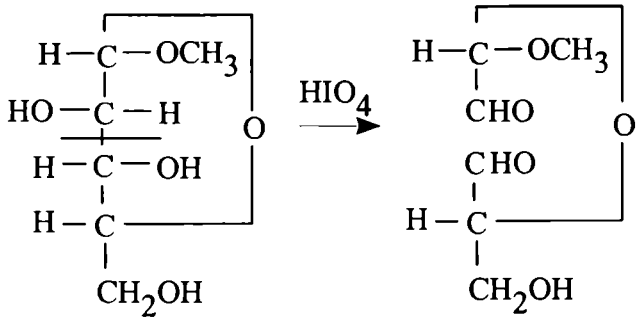
b. 

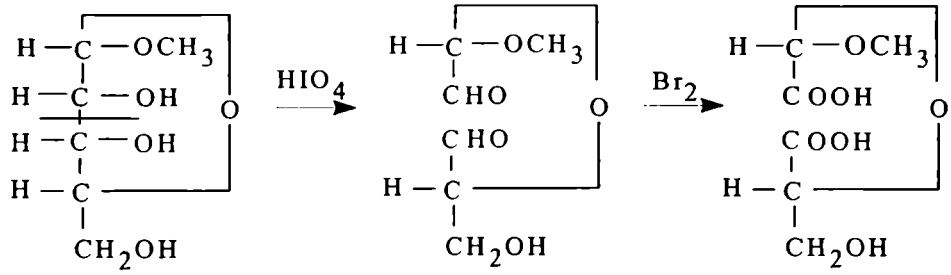
a tetrulose

c. none

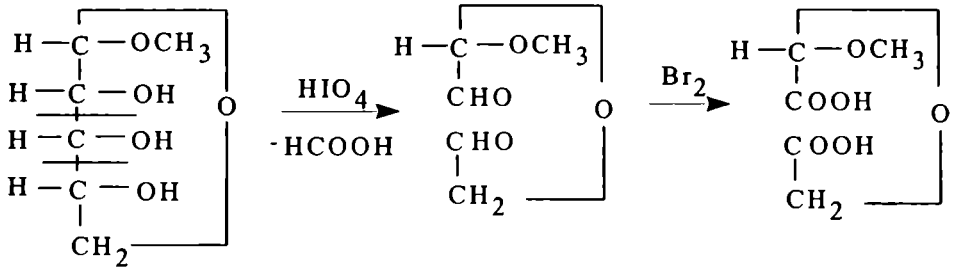
d. 

arabinoside **dialdehyde**

20. Depending on the ring size of the starting sugar, different dialdehyde are obtained upon oxidation with periodic acid. For easier identification the dialdehydes are transformed (bromine oxidation) into diacids (Strontium salts).



α -Omethyl-D -ribofuranoside



α-Omethyl-D -ribopyranoside

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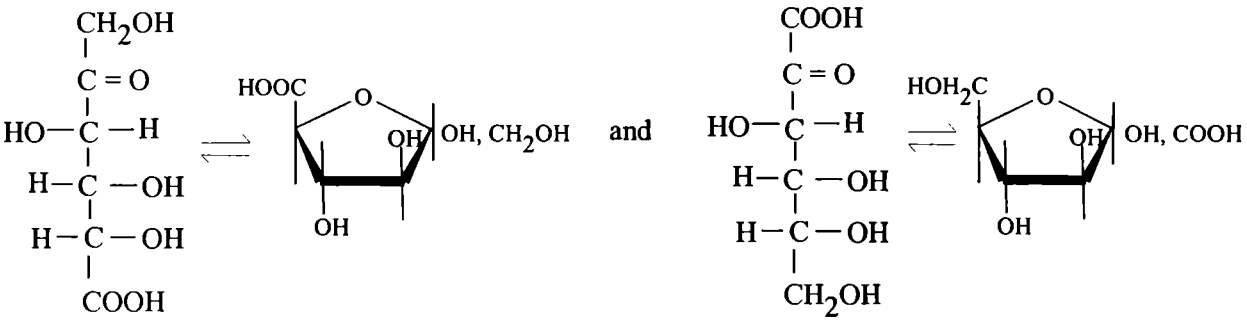
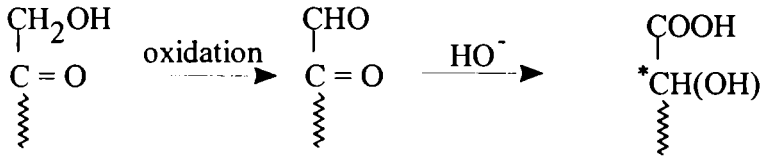
All monosaccharides with pyranosic cycle, from D family will give the same salt, which proove that they have the same configuration at carbon 1 and 5.

21. The structures of the two uronic acids of fructose are presented below:



22. Ketoses are α-hydroxi-ketone and undergo oxidation:



Cannizzaro reaction

26. Ribose and xylose (both D and L configuration) are the aldopentoses which form meso-alditols upon reduction with hydrogen and a catalyst.

27. a. D-altrose

b. L-galactose

28. a. D-tagose

b. D-fructose

29. Allose and altrose, glucose and mannose, gulose and idose , galactose and talose give the same phenylosazones.

30. L-gulose and L-idose are the two aldohexoses that give the same osazone as L-sorbose.

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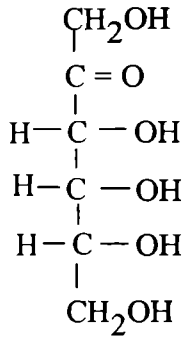
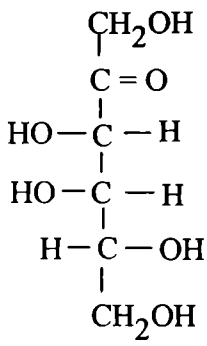
31. The structures of D-psicose and D- tagatose:



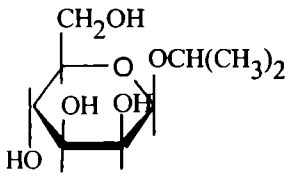
D-psicose



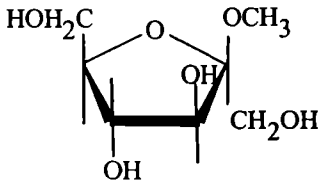
D-tagatose

32.

a.



b.



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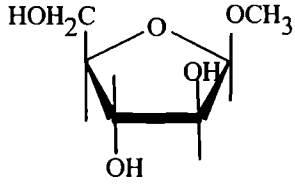

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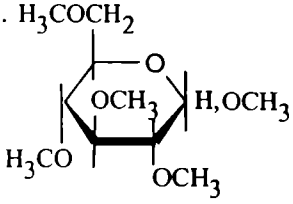

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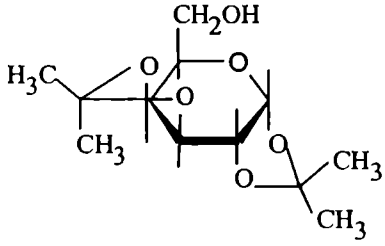

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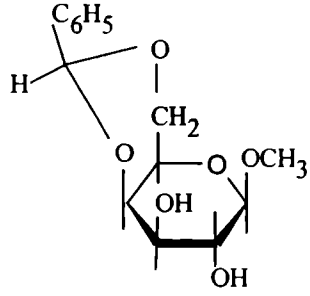

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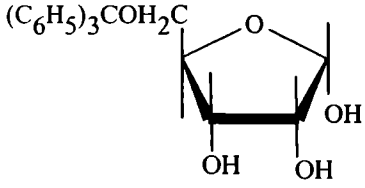

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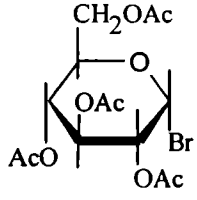

33. **A**: D-altrose, **B**: D-talose, **C**: D-galactose or

A: D-talose, **B**: D-altrose, **C**: D-allose

34. This is the kind of problem that should be solved working backward. **A**: D-talose, **B**: D-galactose, **C**: D-lyxose, **D**: D-threose.

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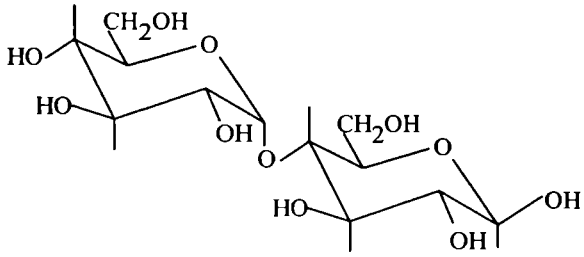
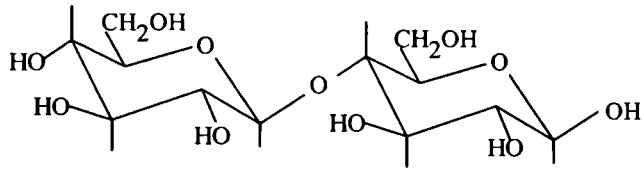
35. β- Cellobiose is more stable because each substituent on each ring is equatorial. The structures of β- maltose and β- cellobiose are given below:



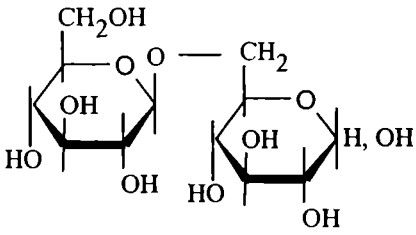
β-maltose



β–cellobiose

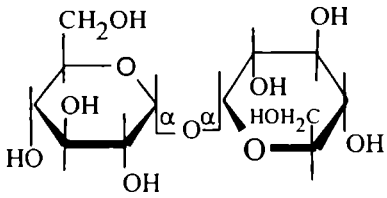
more stable

36.



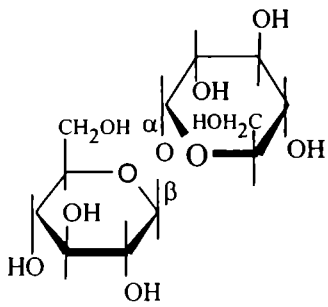
Gentiobiose: 6-(β-D-glucopyranosyl)-D-glucopiranose

37.



Threhalose: α-D-glucopyranosyl-α-D-glucopyranoside

38.



Isothrehalose: β-D-glucopyranosyl-α-D-glucopyranoside

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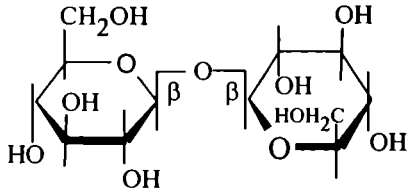
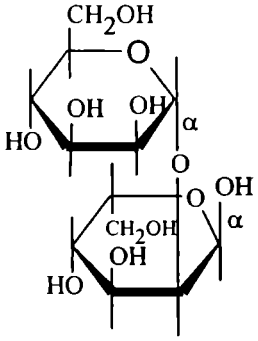


Neothrehalose: β-D-glucopyranosyl-β-D-glucopyranoside

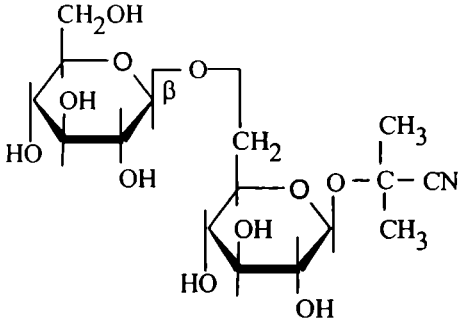
Are nonreducing sugars. Doesn't undergo mutarotation.

40. **Bleomycin** has D-mannose and L-gulose, in pyranosic forms, with α(1,2) glycosidic linkages:



Bleomycin

41.



Linustatin

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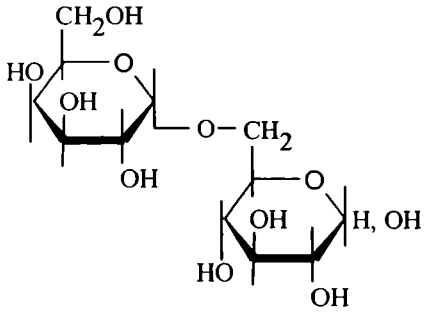
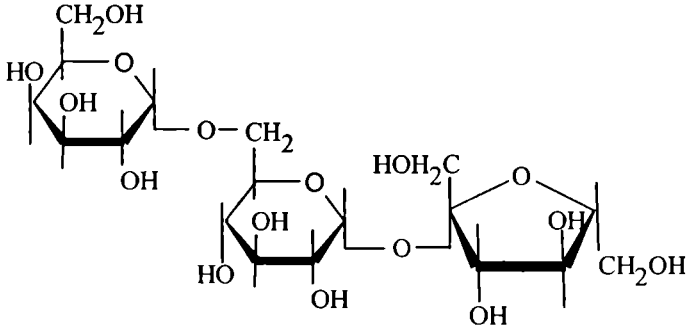
42.

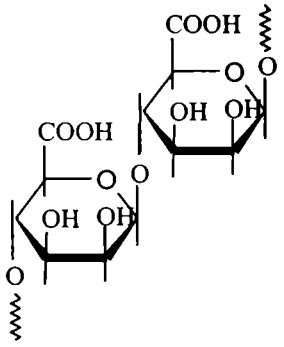


Melibiose



Raffinose

43. a. The structure of alginic acid is prsented below:



Alginic acid

b. 2^4 =16 stereoisomers

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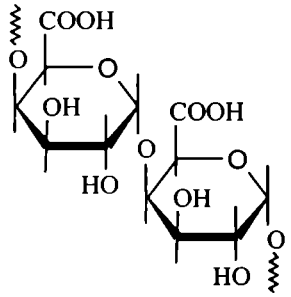
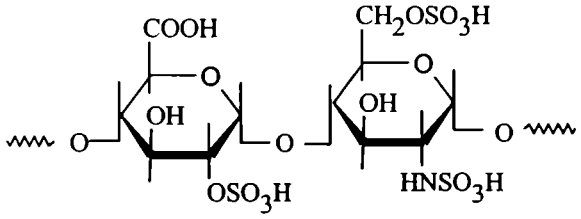
44.



Pectic acid

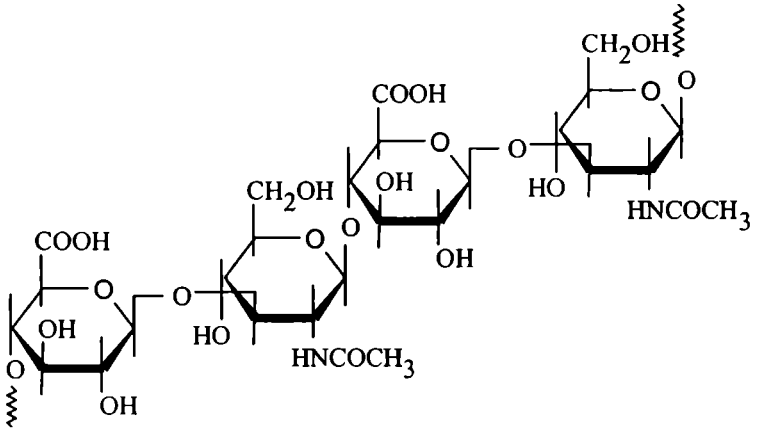
45.



Heparin

(1,4)-O-α-D-glucopyranosyluronic acid-2sulfo-(1,4)-2-sulfamido-2-deoxi-6-O-sulfo-α-D-glucopyranose

46.



Hyaluronic acid

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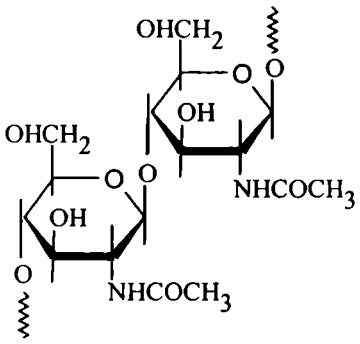
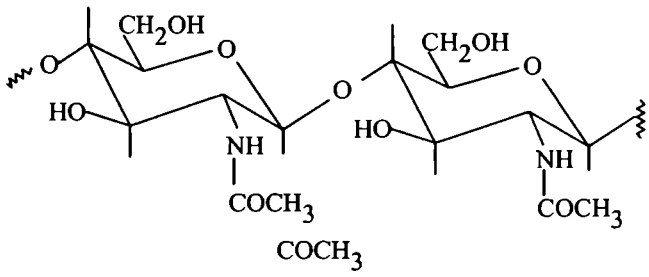
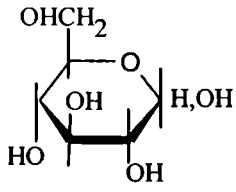
47. Haworth formula and chair conformation of chitin are presented below:





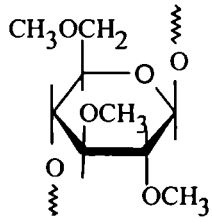
Chitin

49.

a. 

b. no reaction

c. no reaction

d. 

50. a. Proteoglycans are distinguished from the more common glycoproteins by their extremely high carbohydrate content, which may constitute as much as 95% of the dry weight of such molecules. These molecules are found predominantly in the extracellularmatrix of tissues. All proteoglycans contain GAG chains linked to protein molecules (known as core protein) by N- and O-glycosidic linkages.

b. FSH hormone, ribonuclease B

c. lactose, maltose, cellobiose, sucrose, etc

d. Five classes are distinguished: hyaluronic acid, chondroitin sulfate, dermatan sulfate, heparin and keratan sulfate.

51. a. Glycogen stores glucose.

b. Glycosaminoglycans are components of proteoglycans.

c. Glycoconjugates may serve as membrane receptors

d. Protoglycans provide strength, support, and elasticity to tissues.

e. Hormons as FSH and enzymes such as RNAse are glycoproteins

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f. Polysaccharides play important role in the storage of carbohydrate (starch and glycogen) and the structure of plants (cellulose).

52. Although the glycoproteins are sometimes consider to include the proteoglycans, structural reasons seems to be sufficient to examine them separately, such as the relative absence in glycoproteins of uronic acids, sulfate groups, and the disaccharide repeating units that are typical of proteoglycans.

53. Polysaccharides may be divided into two classes: homopolysaccharides, which are composed of one type of monosaccharide (cellulose, starch, glycogen) and heteropolysaccharides, which contain two or more types of monosaccharides (glycoconjugates).

54. Glycoproteins are commonly defined as proteins that are covalently linked to carbohydrate through N- or O-linkages. The carbohydrate groups of glycoproteins are linked to asparagine (Asn) trough an N-glycosidic bond or to the hydroxyl group of serine (Ser) or threonine (Thr). The former glycoprotein class is sometimes referred to as asparagine-linked, the latter is often called mucin-type.

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AMINO ACIDS

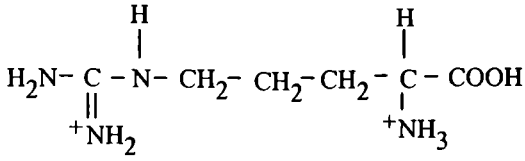
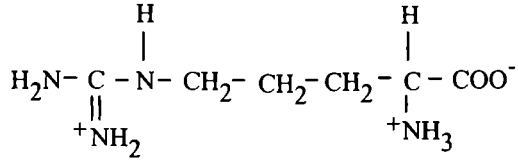
1. Amino acids are classified according to their capacity to interact with water. Four classes may be distinguished: (1) nonpolar and neutral, (2) polar and neutral, (3) acidic, and (4) basic.

2. The side chains (R groups) differ in chemical properties. Some are polar but uncharged, some are polar but have a positive or negative charge in solution. 8 Amino acids have distinctly hidrophobic side chains: Ala, Val, Leu, Ile, Met, Tyr, Phe and Trp.

3. α-amino-isocapronic acid, α-amino-β-hydroxipropionic acid, α-amino succinic acid, α-amino-γ-methylmercaptobutyric acid, α-amino-δ-guanidilvalerianic acid.

4. a. The α carbon is the carbon next to the carboxyl group in the amino acid.
   b. The isoelectric point is the pH at which an amino acid is electrically neutral.
   c. A hydrophobic aminoacid is one with a nonpolar side group.
   d. A peptide bond is an amide bond between two amino acids.
   e. An essential amino acid is an amino acid that cannot be synthesized by the organism.

6. a. The structure and net charge of arginine at various pH level is as follows:

pH	Structure	Net Charge
1		+2
5		+1

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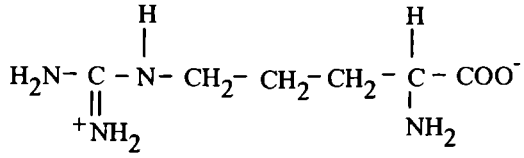
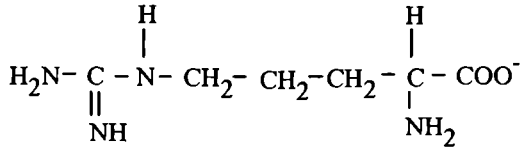
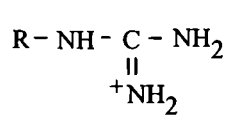
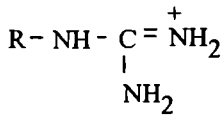
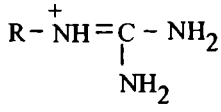
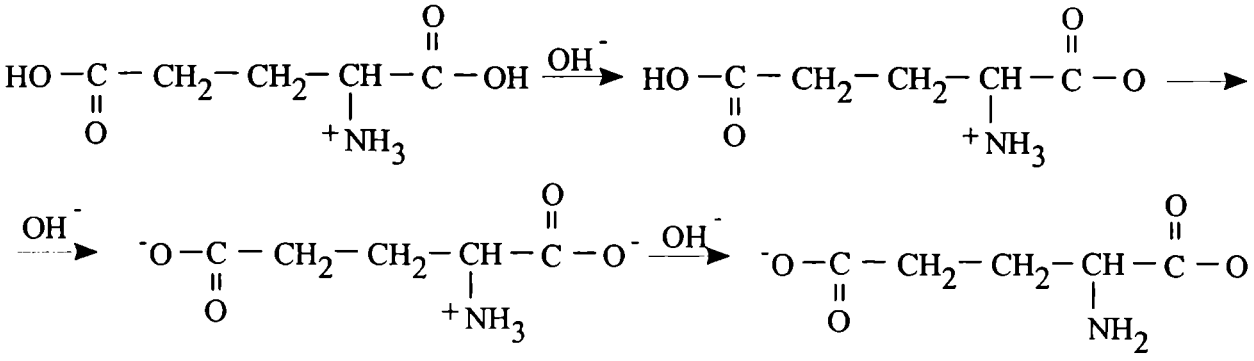
10  0

12  -1

b. pI = 10.76

c.   

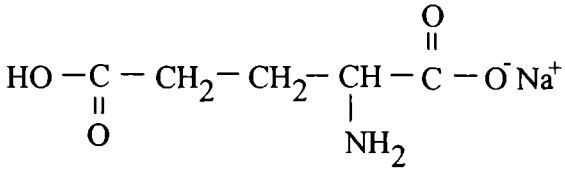
7. a. The ionizable hydrogens are lost in order of acidity, the most acidic ionizing first:



b. pI = 4.25+2.19/2 = 3.22

c. At pH values below the pI, the amino acid is positively charged and moves to the cathode (negative electrode). At pH values above the pI, the amino acid is negatively charged and moves toward the anode (positive electrode). At the isoelectric point the amino acid has no electric charge and therefore does not move in the electric field.

8. The pKa values for glutamic acid: α-carboxyl = 2.19, carboxyl side chain = 4.25



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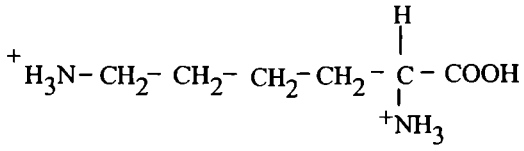
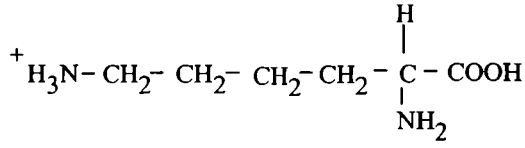
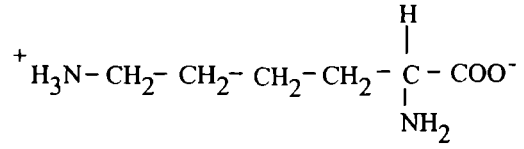
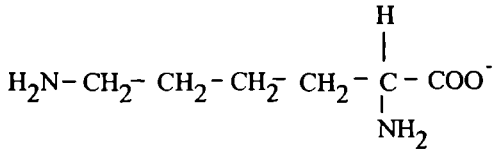
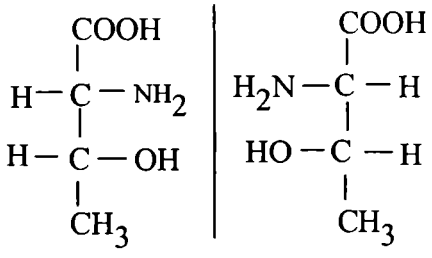
9. b. The structure and net charge of lysine at various pH level is as follows:

pH	Structure	Net Charge
1		+2
4		+1
10		0
12		-1

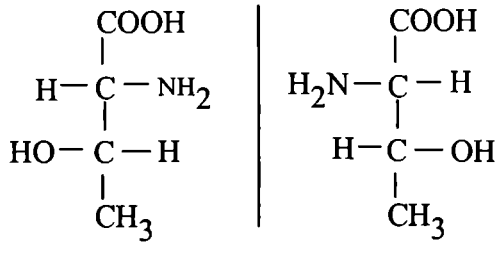
12. At pH=5.7: serine is neutral and is not moving, arginine is positively charged and is moving toward the cathode and aspartic acid, negatively charged is moving toward the anode.

13.The $-CH_2SH$ group has higher priority than does the –COOH group.

14. a. $2^2 = 4$ stereoisomers.



erithro



threo

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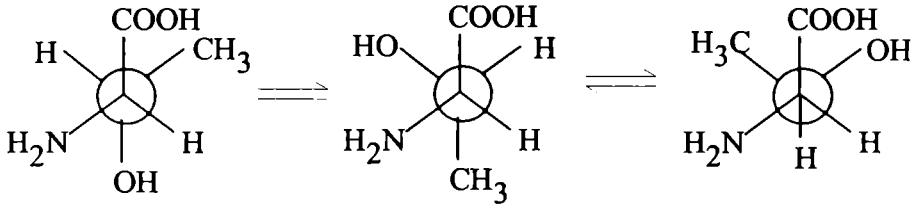
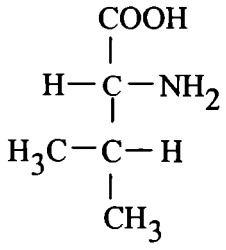
b.

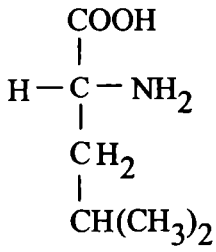


threo, L, natural form

15. a.

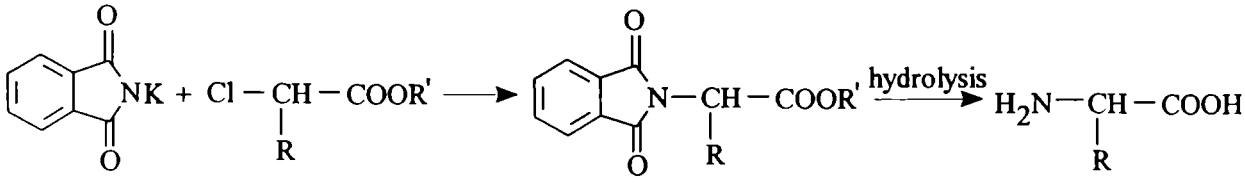


b.



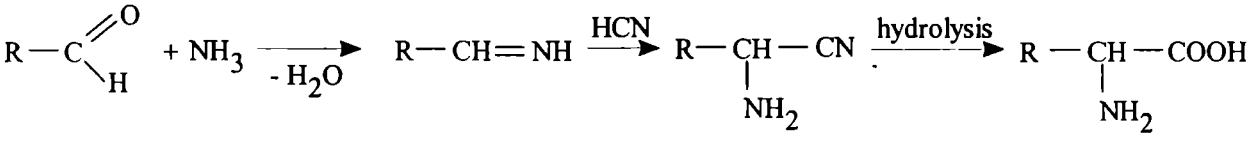
16. Histidine differs from proline in: size: His is only slightly larger than Pro. Both are medium-sized. Shape: Because His is aromatic, its five-membered ring is planar. The aliphatic Pro side chain is a puckered five-membered ring. Polarity: The Pro R-group is always apolar, whereas the basic His imidazol ring is charged and polar below its pK_a and apolar above its pK_a.

17. Gabriel phtalimide synthesis:



where R is: a.- H, b. - CH_3, c. C_6H_5 - CH_2^-

18. The Strecker synthesis of amino acids is a two-step sequence. The first step is the reaction of an aldehyde with a mixture of ammonia and HCN to yield an aminonitrile. Hydrolysis of ths aminonitrile results in the amino acid:



where R is: a. – H, b. – CH_3, c. – CH_2 – C_6H_5.

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19.

a. $CH_3Cl + {}^{-}:C(COOR)_2(NH-COCH_3) \longrightarrow CH_3-CH(COOR)_2(NH-COCH_3) \longrightarrow CH_3-CH(NH_2)-COOH$

alanine

b. $C_6H_5-CH_2-Cl + {}^{-}:C(COOR)_2(NH-COCH_3) \longrightarrow C_6H_5-CH_2-CH(COOR)_2(NH-COCH_3) \longrightarrow C_6H_5-CH_2-CH(NH_2)-COOH$

phenylalanine

c. $ROOC-CH=CH_2 + {}^{-}:C(COOR)_2(NH-COCH_3) \longrightarrow ROOC-CH_2-CH_2-CH(COOR)_2(NH-COCH_3) \longrightarrow$

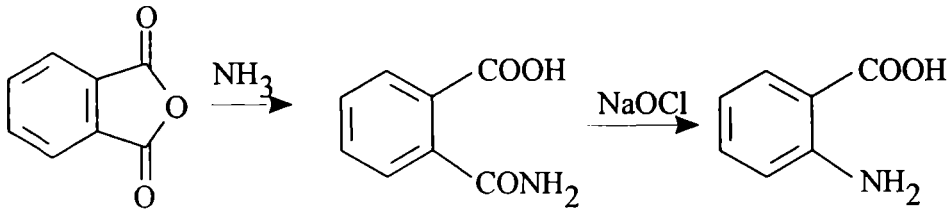
$\longrightarrow ROOC-CH_2-CH_2-CH(NH_2)-COOH$

glutamic acid

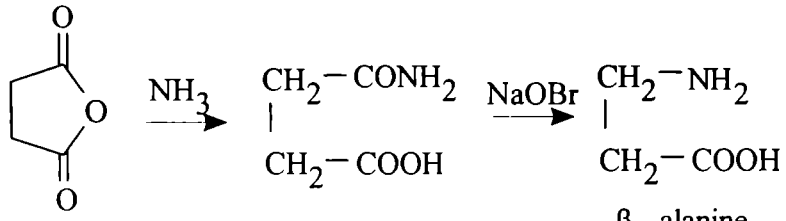
d. $CH_2=O + {}^{-}:C(COOR)_2(NH-COCH_3) \longrightarrow HO-CH_2-CH(COOR)_2(NH-COCH_3) \longrightarrow HO-CH_2-CH(NH_2)-COOH$

serine

20. β- Amino acids can be obtained through Hoffman degradation of monoamide of 1,4-dicarboxylic acids:



Antranilic acid



β– alanine

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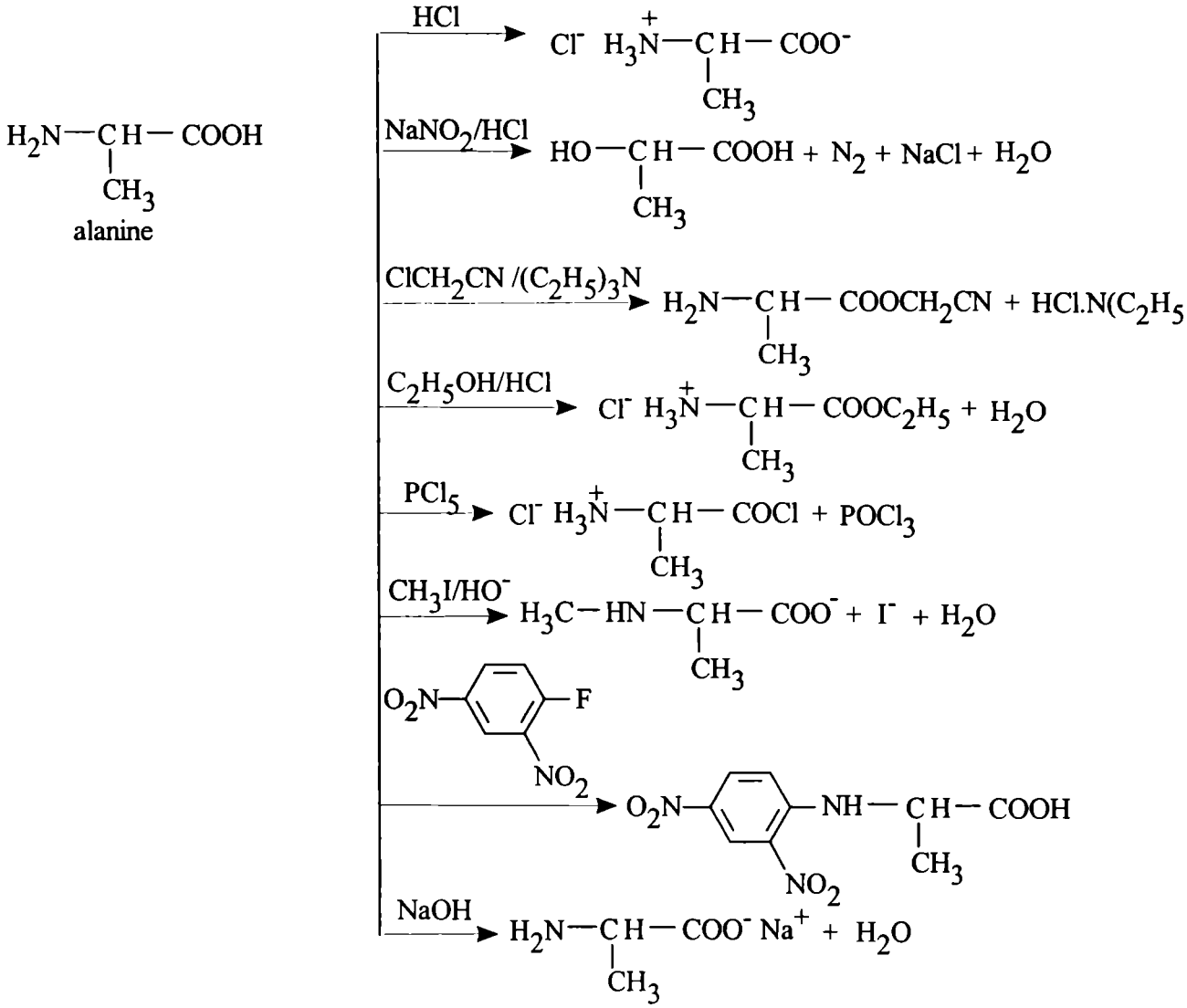
23. a. L-Ala, L-Asp, L-Glu

b. L- and D-Ala, L- and D-Asp, L- and D-Glu.

24. Most amino acids contain primary amino groups, which can form the imine group in Ruhemann's purple. Proline and hydroxiproline contain a secondary amino group, which cannot form am imine.

28. Benzyl esters, benzyl ethers and benzyloxycarbonyl group can be deprotected via hydrogenolysis in the presence of10% palladium-on charcoal catalyst.

29.



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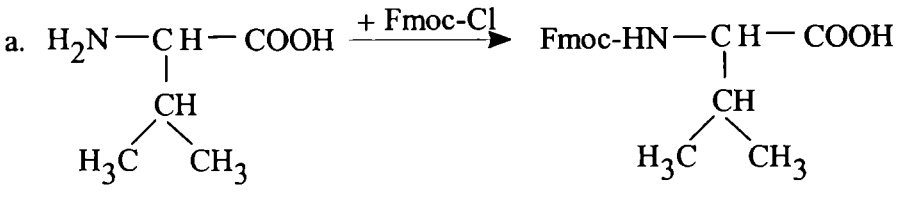
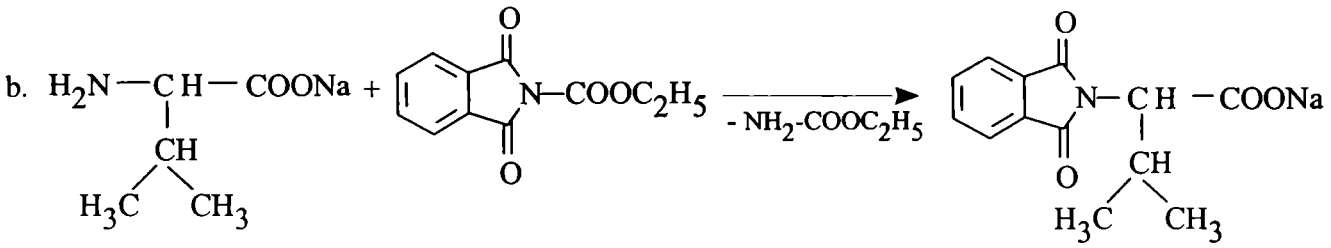
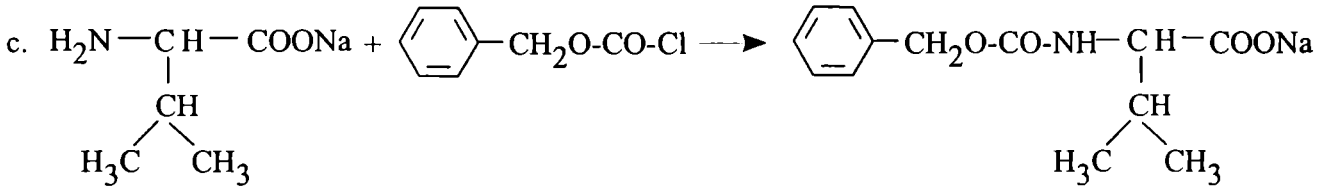
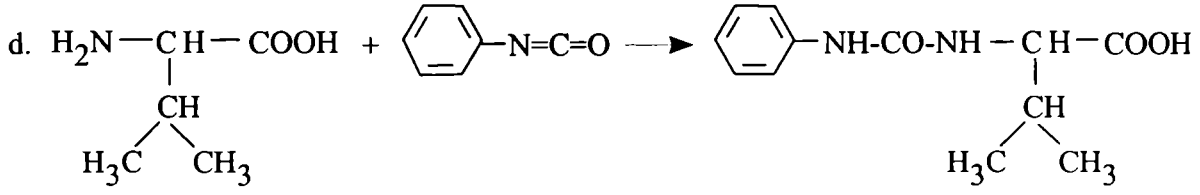
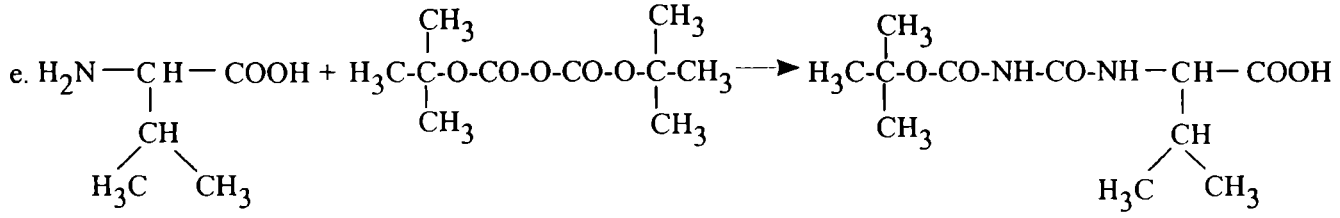
30.

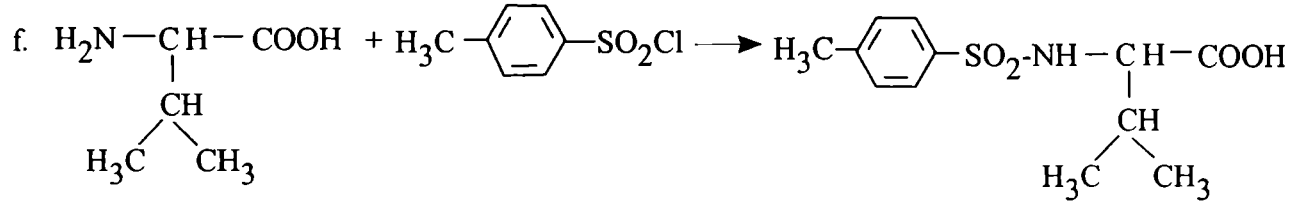
a. 

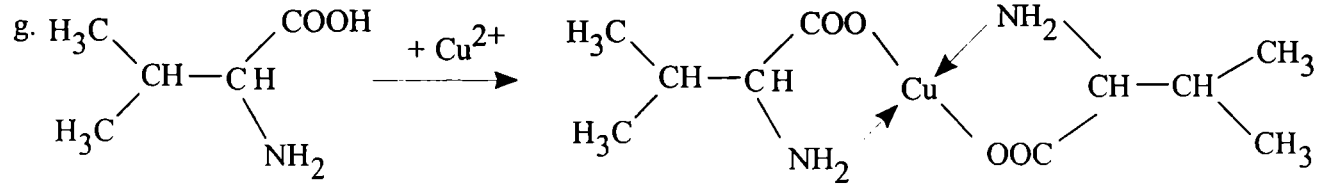
b. 

c. 

d. 

e. 

f. 

g. 

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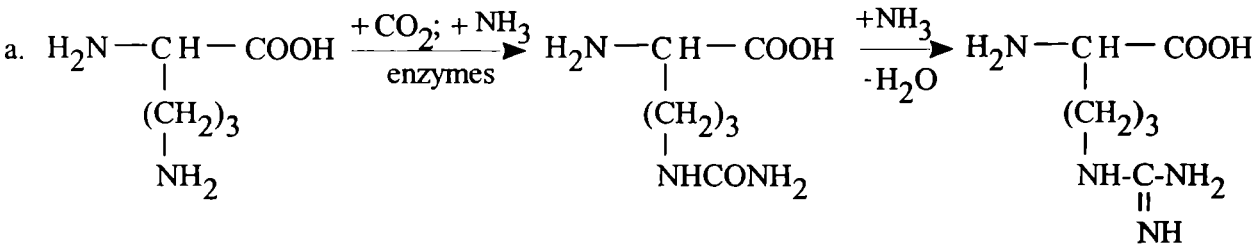
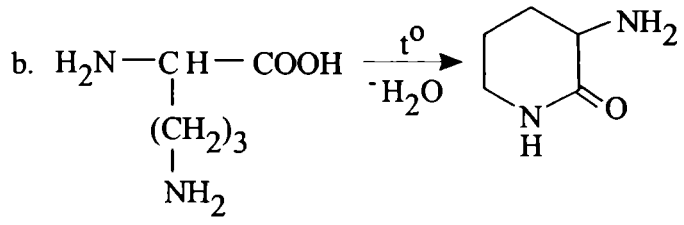
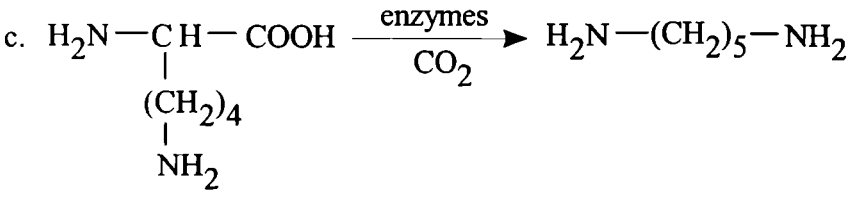
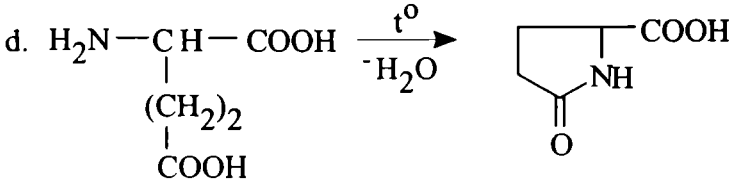
31.

a. 

b. 

c. 

d. 

32. The branched-chain amino acids (leucine, isoleucine and valine) are metabolized in tissues, such as muscle, where they are principally used to synthesize nonessential amino acids.

33. The metabolic products of amino acids degradation are acetyl-CoA, acetoacetyl-CoA, pyruvate, α-ketoglutarate, succinyl-CoA, fumarate, and oxaloacetate.

34. Despite the complexity of amino acid degradative pathways, the following general statements can be made. The catabolism of amino acids usually begins by removing the amino group. Amino groups can then be disposed of in ureea synthesis. The carbon skeletons produced from the standard amino acids are then degradated to form seven metabolic products: acetyl-CoA, acetoacetyl-CoA, pyruvate, α-ketoglutarate, succinyl-CoA, fumarate, and oxaloacetate. Depending on the animal's current metabolic requirements, these molecules are used to synthesize fatty acids or glucose or to generate

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energy. Amino acids degradated to form acetyl-CoA or acetoacetyl-CoA are referred to as **ketogenic** because they can be converted to either fatty acids or ketone bodies. The carbon skeletons of the **glucogenic** amino acids, which are degradated to pyruvate or a citric acid cycle intermediate, can then be used in gluconeogenesis.

Glucogenic amino acids: tyrosine, lysine, valine

Ketogenic amino acids: tyrosine, lysine, glycine, alanine, threonine.

35. The following amino acids are both ketogenic and glucogenic: phenylalanine, isoleucine, lysine, tryptophan, and tyrosine.

36. The nonessential amino acids (NAA) are synthesized from readily avaible metabolites. Alanine, arginine, asparagine, aspartate, cysteine, glutamate, glutamine, histidine, proline, serine, tyrosine are NAA. Arginine is normally synthesized by the ureea cycle. In small children, the ureea cycle is not fully functional. Consequently, arginine must be obtained from external sources.

37. If lysine were transaminated, ε amino group of the new keto acid (derived from lysine) would cyclize to form an intramolecular Schiff base. Consequently, the α-keto acid required to produce lysine by transamination cannot exist in appreciable quantities. Therefore lysine cannot be produced by this reaction.

38. Glutamate is synthesized from α-ketoglutarate by to means: (1) transamination, catalyzed by the aminotransferases (pyridoxal phosphate is a required coenzyme) and (2) direct amination, catalyzed by glutamate dehydrogenase. NADPH provides the reducing power for this reaction.

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1. A protein is a polymer containing more than 50 amino acid residues comprising one or more polypeptide chains. A peptide is a polymer containing less thaan 50 amino acid residues. A polypeptide is a polymer containing greater than 50 amino acids.

2. Because of their diversity, proteins are often classified in two ways, based on their shape and their composition.
   a. Fibrous proteins are long, rod-shaped molecules that are insoluble in water and physically tough. Keratins found in skin, hair and nails, have structural and protective functions. Globular proteins are compact spherical molecules that are usually water-soluble. Typically, globular proteins have dynamic functions.
   b, c. Simple proteins, such as serum albumin and keratin, contain only amino acids. In contrast, each conjugated protein consists of a simple protein combined with a nonprotein component. The nonprotein component is called a prosthetic group. A protein without its prosthetic group is called an apoprotein. A protein molecule combined with its prosthetic group is referred to as a holoprotein.

4. Salting out is a technique in which high concentrations of salts such as amonium sulfate [$(NH_4)_2SO_4$] are used to precipitate proteins. As a protein becomes more pure more sophisticated methods are used to achieve further purification. The most commonly used techniques include chromatography and electrophoresis.
   Three chromatographic methods commonly used in protein purification are ion-exchange chromatogrphy, gel-filtration chromatography, and affinity chromatography.
   Ion-exchange chromatography separates proteins on the basis of their charge. Anion-exchange resins, which consist of positively charged materials, bind reversibly with a protein's negatively charged groups. Similarly, cation-exchange resins bind positively charged groups. After proteins that do not bind to the resin are removed, the protein of interest is recovered by an appropriate change in the solvent Ph and/or salt concentration.
   In gel-filtration chromatography, a column packed with a gelatinous polymer separates molecules accoding to their size and shape. Molecules that are larger than the gel pores are excluded and therefore move through the column quikly. Molecules that are smaller than the gel pores diffuse in or out the pores, so their movement through the colmn is retarded.

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Differences in these rates separate the protein mixture into bandds, which are then collected separately.

Affinity chromatography uses a special noncovalent binding affinity between the protein and the ligand. The ligand is covalently bound to an insoluble matrix, which is placed in a column. After nonbinding protein molecules have passed through the column, the protein of interest is removed by altering the conditions that affect binding (pH or salt concentration).

In electrophoresis, proteins separate from other molecules, in an elctric field because of differences in their net charge. Molecules with a positive net charge migrate toward thenegativelycharged electrode (cathode). Molecules with a net negative charge will move toward the anode. Molecules with no net charge will not move at all. Electrophoresis is nearly always carried out by using gels such as polyacrylamide. Bands resulting from a gel electrophoretic separation may be treated in sevaral ways. During purification, specific bands may be excised from the gel after visualization with ultraviolet light. Each protein-containing slice is then eluted with buffer and prepared for the next step.

5. Proteins have the most diverse functions in the body: catalysis, structure, mouvement, defense, regulation, transport.

6. a. heat – hydrogen bonding (secondary and tertiary structure)
   b. strong acid - hydrogen bonding and salt bridges (secondary and tertiary structure)
   c. saturated salt solution – salt bridges (tertiary structure)
   d. organic sovents(alcohol) – hydrofobic interactions (tertiary structures)
   e. Mercury (Hg^{2+}) and lead (Pb^{2+}) may disrupt salt bridges by forming ionic bonds with negatively charged groups or may bind to sulfhydryl groups (tertiary structure)

7. The α-helix is a rigid, rodlike structure that forms when a polypeptide chain twists into a right-handed helical conformation. Because of several structural constraints (rigidity of peptide bonds and the allowed limits on the values of the ϕ and ψ angles) certain amino acids do not foster α-helix formation. For example, glycine's R group (a hydrogen atom) is so small that the polypeptide chain may be to flexible.

10. c.

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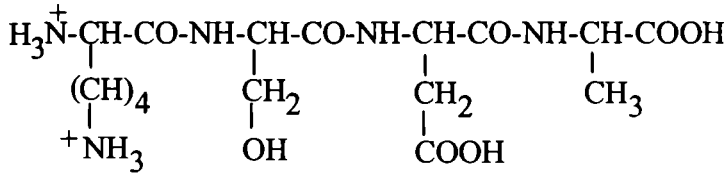
11. The following types of interactions stabilize tertiary structure: hydrophobic interactions, electrostatic interactions, hydrogen bonds, covalent bonds.

12. Amino acids with basic side groups such as lysine, arginine or tyrosine would contribute to a high pI value.

14. a. The structure of the tetrapeptide in its most acidic form is shown below:



Both lysine and aspartic acid have ionizable side chains in addition to containing terminal α-amino and α-carboxyl groups, respectively. The pK_a values are the follows:

Lysine: α-amino = 8.95, amino side chain = 10.79

Aspartic acid: carboxyl side chain = 3.86

Alanine: α-carboxyl = 2.34

The electrically neutral peptide is formed after both carboxyl groups have lost their protons but before either ammonium group has lost any protons. The isoelectric poin is calculated as follows:

$$pI = 3.86 + 8.95/2 = 12.81/2 = 6.4$$

b. At pH = 4 the peptide is positively charged and moves toward the negative electrode (cathode). At pH = 9 the peptide is negatively charged and will move toward the positive electrode (anode).

15. The structures of the dipeptides are shown below:

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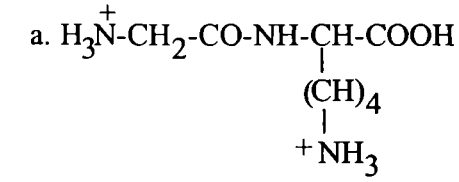
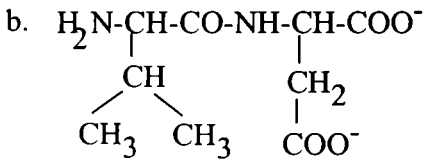
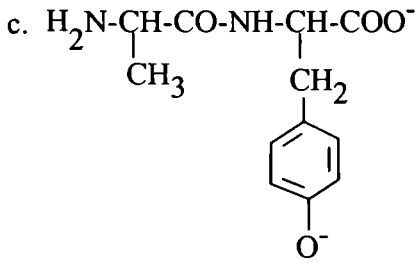
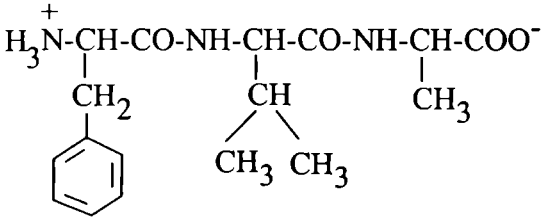
a. 

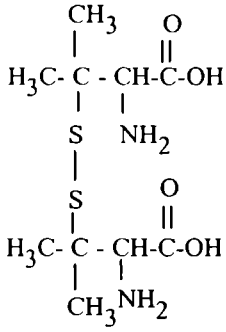
b. 

c. 

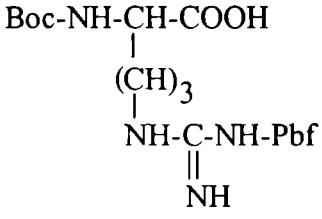
16. The structure of the tripeptide at isoelectric point is:

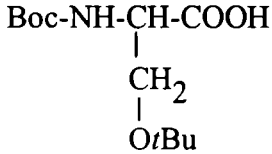


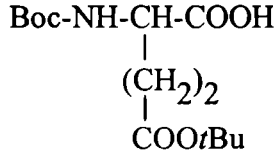
17.

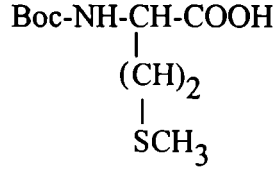


21. The amino acids used for synthesis of the tetrapeptide are the following:









Boc protocol for SPPS:

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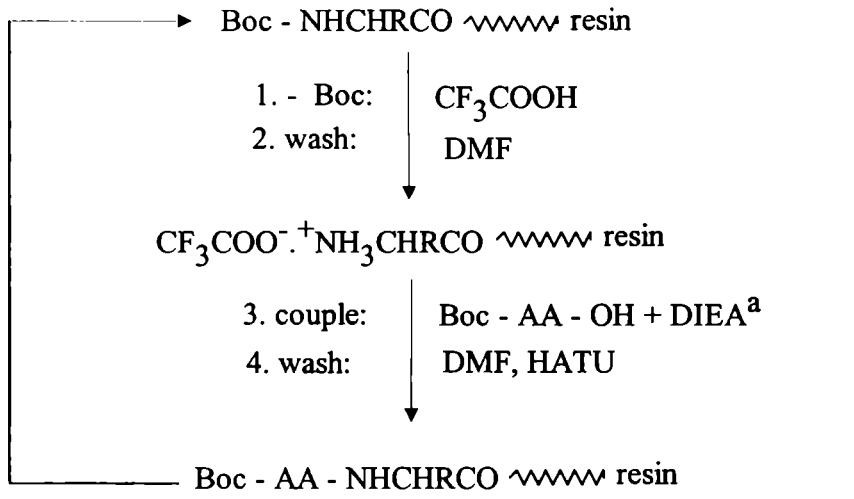
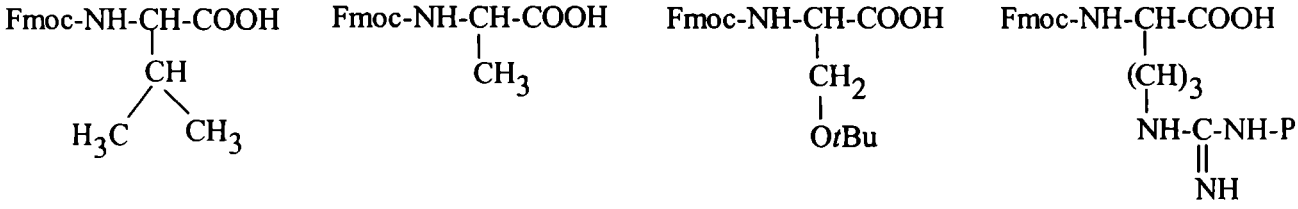
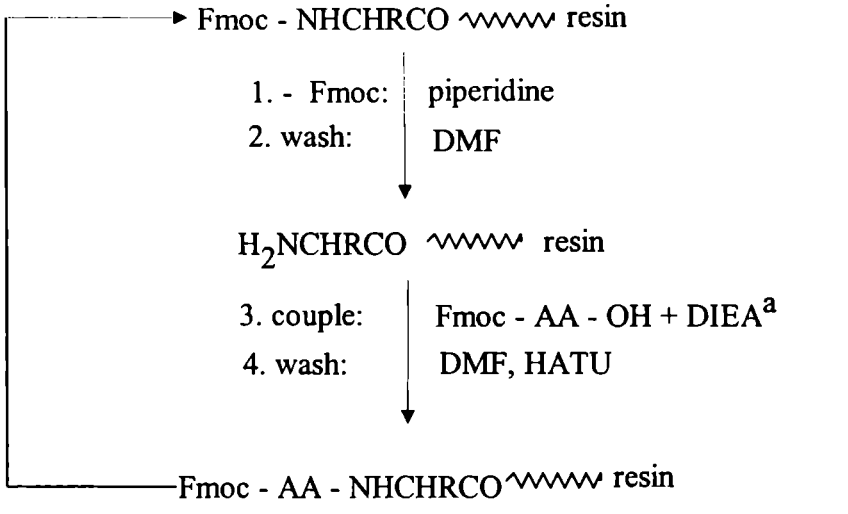


a. AA - amino acid; DIEA - Diisopropylethylamine

22. The amino acids used for synthesis of the tetrapeptide are the following:



Fmoc protocol for SPPS:



a. AA - amino acid; DIEA - Diisopropylethylamine

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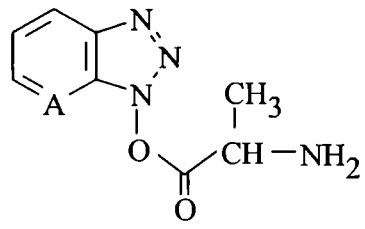
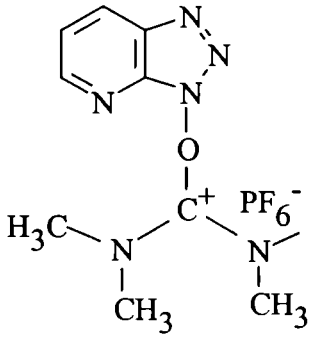
24.

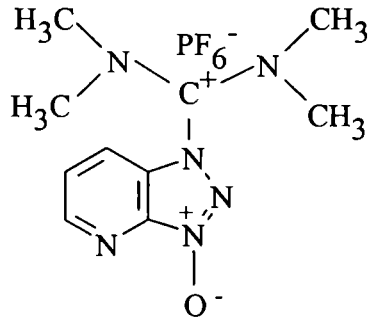


A = CH, N

25.

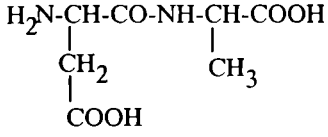


O-HATU

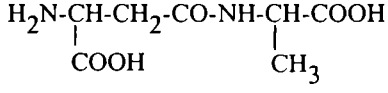


N-HATU

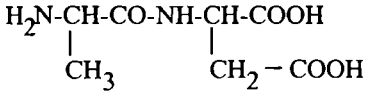
26. There are six dipeptides: Asp-Ala, βAsp-Ala, Ala-Asp, Asp-Asp, βAsp-Asp, Ala-Ala.



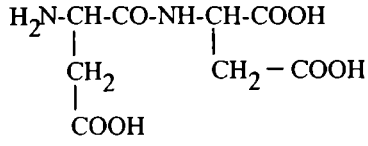
Asp-Ala



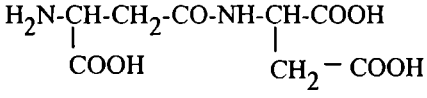
βAsp-Ala



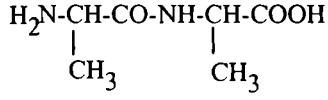
Ala-Asp



Asp-Asp



βAsp-Asp



Ala-Ala

27. There are six tetrapeptides: Phe-Ser-Ala-Leu, Phe-Ser-Leu-Ala, Ala-Ser-Leu-Ala, Leu-Ala-Phe-Ser, Ala-Phe-Ser-Leu, Leu-Phe-Ser-Ala.

28. a. $20^8 = 25{,}600{,}000{,}000$

b. 20^{100}

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29. a. Trypsin cleaves the amide bond (to the right) of lysine and arginine.

trp - met - gly - ile - phe - arg / phe - trp - val - lys / ala - met - ser $\xrightarrow[H_2O]{\text{trypsin}}$

trp - met - gly - ile - phe - arg + phe - trp - val - lys + ala - met - ser

b. Chymotrypsin cleaves the amide bond (to the right) of tyrosine, phenylalanine, tryptophan.

trp / - met - gly - ile - phe / arg - phe / trp / val - lys - ala - met - ser $\xrightarrow[H_2O]{\text{chymotripsin}}$

2trp + met - gly - ile - phe + arg - phe + val - lys - ala - met - ser

c. Pepsin cleaves the amide bond (to the left) of tyrosine, phenylalanine, tryptophan.

trp - met - gly - ile / phe - arg / phe / trp - val - lys - ala - met - ser $\xrightarrow[H_2O]{\text{pepsin}}$

trp - met - gly - ile + phe - arg + phe + trp - val - lys - ala - met - ser

d. Thermolysin cleaves the amide bond (to the left) of isoleucine, leucine, valine

trp - met - gly / ile - phe - arg - phe - trp / val - lys - ala - met - ser $\xrightarrow[H_2O]{\text{thermolysin}}$

trp - met - gly+ ile - phe - arg - phe - trp + val - lys - ala - met - ser

e. Cyanogen bromide cleaves the amide bond (to the left) of methionine

trp - met / gly - ile - phe - arg - phe - trp - val - lys - ala - met / ser $\xrightarrow[H_2O]{\text{cyanogen bromide}}$

trp - met + gly - ile - phe - arg - phe - trp - val - lys - ala - met + ser

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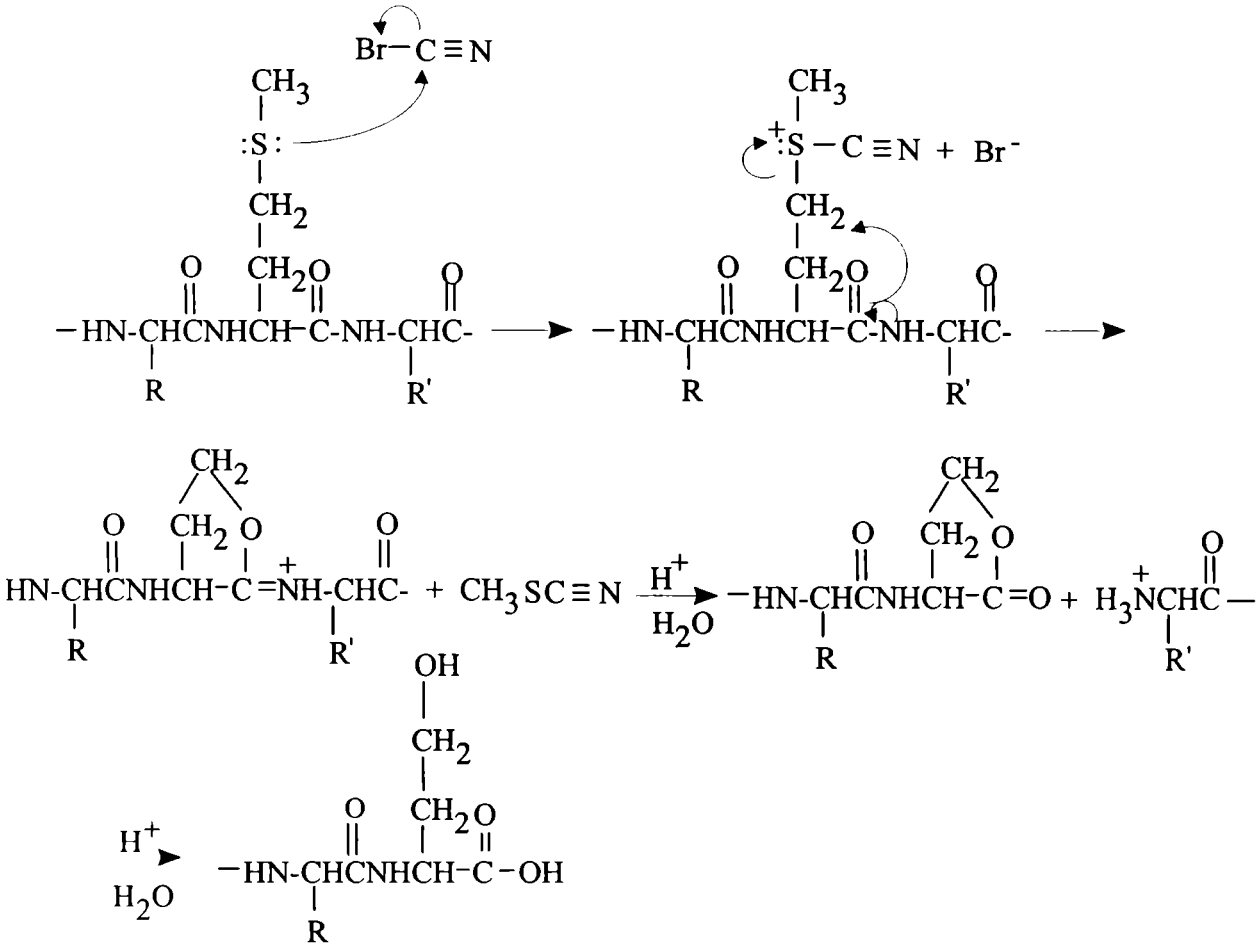
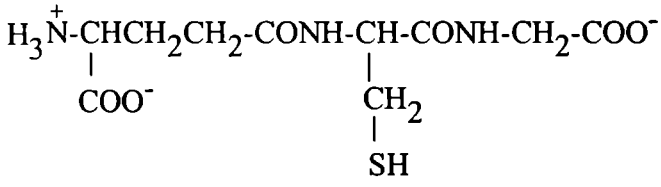
30. The mechanism for the cleavage of a peptide bomd by cyanogen bromide is:



31. b. The structural formula of glutathione is:



33. H-Trp-Val-Glu-Ser-Arg-OH.

34. a. The structures of Met-enkephalin at pH 7 and 12 are given below:

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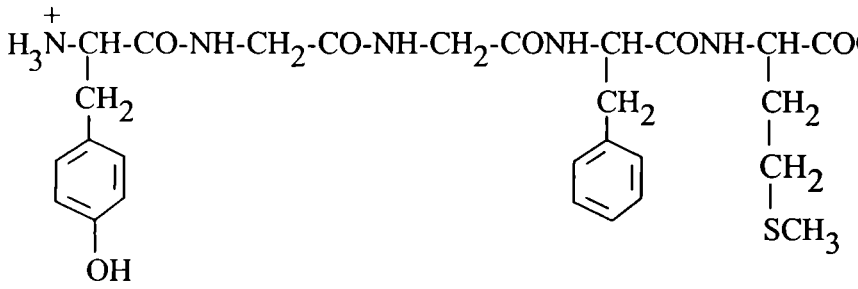
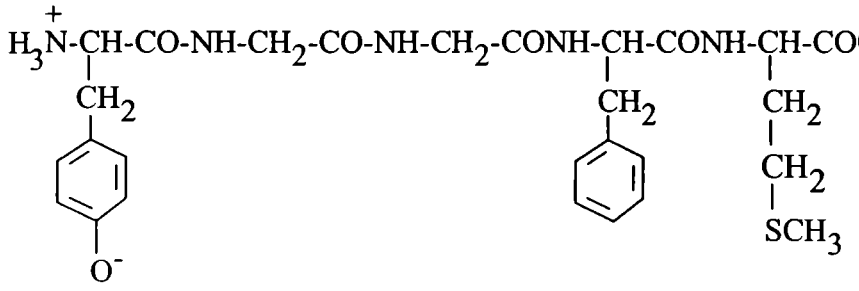
pH	Structure	Net charge
7		0
12		-1

b. Tyr, Gly-Gly-Phe, Met are obtained when Met-enkephalin is treated with chymotrypsin
Tyr-Gly-Gly, Phe-Met are obtained when Met-enkephalin is treated with pepsin

35. Tyr-Gly-Gly-Phe-Leu
Tyr-Gly-Gly-Phe, Leu are obtained when Leu-enkephalin is treated with thermolysin
Tyr-Gly-Gly, Phe-Met are obtained when Leu-enkephalin is treated with pepsin

36. b.

37. ACP: H-Val-Gln-Ala-Ala-Ile-Asp-Tyr-Ile-Asn-Gly-OH

38. a. $(Tyr)_{10}$ is less soluble than Tyr because the peptide has nine additional hydrophobic side chain, but only the same two charged groups.
b. A pH >11.1 would increase solubility of Tyr (or $(Tyr)_{10}$) because the R groups would be charged (pKa = 10.1). Choose a pH higher than pKa+1.

39. b.

40. Bradykinin: H-Arg-Pro-Pro-Gly-Phe-Ser-Pro-Phe-Arg-OH

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41. The following fragments are produced when bradykinin is treated with the indicated reagents:

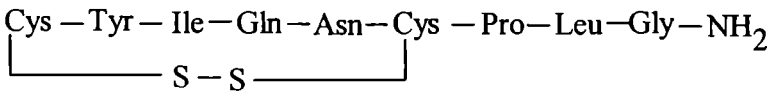
    a. Arg and Arg-Pro-Pro-Gly-Phe-Ser-Pro-Phe

    b. Arg-Pro-Pro-Gly-Phe, Ser-Pro-Phe, and Arg

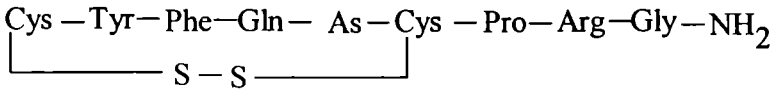
    c. Arg and Pro-Pro-Gly-Phe-Ser-Pro-Phe-Arg

    d. DNP-Arg and the following amino acids residues 3 Pro, 1 Gly, 2 Phe, 1 Ser, 1 Arg.

42. The primary structure of oxytocin is:



43. The primary strycture of vasopressin is:



44. Gly-Arg-Trp-Ala-Glu-Leu-Met-Pro-Val-Asp

45. Lys-Ser-Glu-Leu-Trp-Lys-Ser-Val-Glu-His-Gly-Ala-Met

46. Glu-Gly-Pro-Trp-Gly-Trp-Leu-Glu-Glu-Glu-Glu-Ala-Ala-Tyr-Met-Asp-Phe or Glu-Gly-Pro-Trp-Leu-Glu-Glu-Glu-Glu-Ala-Ala-Tyr-Gly-Trp-Met-Asp-Phe

47. The structure of β-endorphin is: Tyr-Gly-Gly-Phe-Met-Thr-Ser-Glu-Lys-Ser-Gln-Thr-Pro-Leu-Val-Thr-Leu-Phe-Lys-Asn-Ala-Ile-Val-Lys-Asn-Ala-His-Lys-Lys-Gly-Gln.

48. Amino acids 1-14 and 19-28 are likely to form helices. Proline generally is not found in helices because it is unable to rotate appropoately about one of its peptide bond. Glycine also is rarely found in helices.

49. 110 A in an α-helix and 260 A in a straight chain.

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